The Centers for Disease Control and Prevention

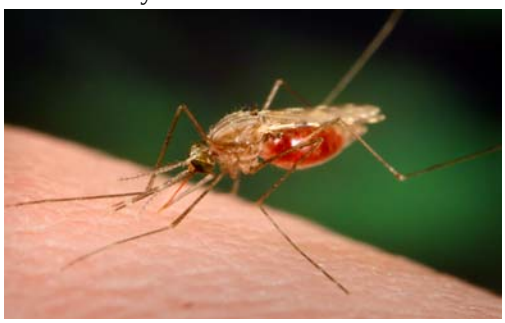
SAFER • HEALTHIER • PEOPLE™

CONTENTS

AGRICULTURAL AND ENVIRONMENTAL

Pest Control

Compounds for Pest Control and Methods for their Use
The control of public health pests is critical for preventing numerous vector borne diseases throughout the world. New insecticidal compounds and application strategies are needed to protect both public health and the environment, and to combat chemical resistance. In this invention, biologically active fractions of essential oil of Alaska yellow cedar have been identified which are insecticidal and acaricidal. These natural compounds were found to be active for up to 11 weeks against the tick vector, *Ixodes scapularis*; the mosquito vector, *Aedes aegypti*; and the flea vector, *Xenopsylla cheopsis*.



Inventors: Gary Maupin, Joe Karchesy, Nicholas Panella
CDC Reference Number: I-024-00
Publication Number: WO0250053

A Simple Process for Producing Wash-Durable Insecticide Impregnated Bednets or Other Fabrics
In developing countries where diseases such as malaria are prevalent, the use of insecticide impregnated bednets is an effective means for reducing morbidity and mortality of insect borne diseases. However, current procedures for impregnating bednets last only 1-2 washes before re-impregnation is needed. This invention improves the insecticide impregnation process resulting in the production of a bednet that remains sufficiently effective at killing and repelling disease vector mosquitoes/insects after 6-10 washes.

Inventors: Michael Green, Dwight Mount
CDC Reference Number: I-008-99
Patent Number: 6,896,892

Simple, Nondestructive Colorimetric Field Method to Identify and Quantify Cyanopyrethroid Insecticides
This invention encompasses a method to quickly and easily test pyrethroid-impregnated mosquito netting (bednets) for effectiveness. These types of netting are used to combat malarial transmission from disease-transmitting mosquitoes. After extended use or washing, these nets lose the insecticide properties and must be retreated. This simple, nondestructive test reacts to chemicals in the pyrethroid netting treatment to allow field workers to determine a net's effectiveness in thirty minutes with an easy to read color change.

Inventor: Michael D. Green
CDC Reference Number: I-033-05

Synergistic Combinations of Natural Plant Extracts to Control and Repel Arthropod Pests
The compounds, compositions, and methods that employ a monoterpene, carvacrol, used in combination with eremophilane sequiterpenes to control and repel arthropod pests have been evaluated. These natural plant compounds have been demonstrated to be more effective when used in combination than when used individually in laboratory bioassays against ticks, fleas, and mosquitoes. These compounds have minimal adverse effects on humans, animals, and the environment. These compounds may be isolated from natural sources (ex. Alaska yellow cedar), semi-synthesized from naturally occurring compounds, or completely synthesized. The compounds may be applied directly to pests, pest habitats, and function as a topical or ingestible toxin."

Inventors: Marc Dolan, Gary Maupin, Nicholas Panella, Joe Karchesy, EB Gabrielle Dietrich
CDC Reference Number: I-028-04
Publication Number: 20050187289

Air Quality

Air Sampler for Collecting Airborne Fungal Spores in a Microcentrifuge Tube for Molecular Analysis
A sampling apparatus that utilizes one or more cyclone separators to collect airborne particles from the atmosphere. The apparatus' function is not only to separate out aerosols from the atmosphere but to also serve as a collection tube for the aerosol particles. Through its unique design the apparatus is able to use the centrifugal force of the air flow on the particles forcing them to separate. Since the sample is collected directly in the collection tube, in situ analysis of the collected particles can be

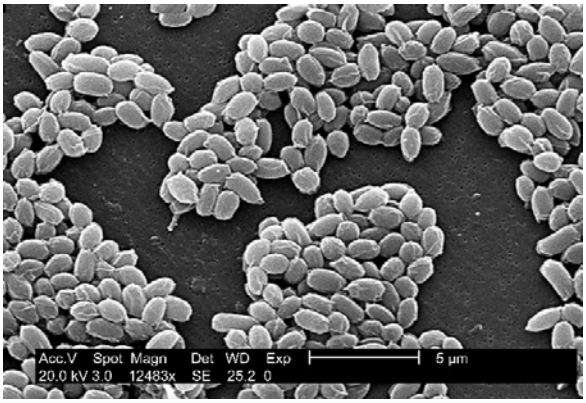
performed. Analysis may include, but is not limited to, PCR, immunoassay analysis, microscopic spore counting, and counting colony-forming units.

Inventors: Teh-hsun "Bean" Chen, Gregory Feather, Jyoti Keswani, Herbert Edgell
CDC Reference Number: I-020-03
Publication Number: WO2005040767

BACTERIAL

Bacillus anthracis

Mass Spectrometry-Based Detection Assay for Anthrax Lethal Factor and Lethal Toxin Activity
This invention identifies an assay for extremely fast and sensitive detection of *Bacillus Anthracis* lethal toxin (LTx), the toxin responsible for the lethal effects of anthrax infection. This assay has already been successfully tested in animals and will allow for early detection of anthrax infection and screening of lethal factors to monitor anthrax infections, such as for vaccine trial candidates. LTx is composed of two proteins, protective antigen (PA) and lethal factor (LF). The assay effectively detects LF by first using magnetic protein G beads to capture and concentrate LF in samples, then testing for LF on the bead by reacting it with a peptide substrate designed to mimic LF's natural target. By testing its reaction to and cleaving of this peptide substrate with mass spectrometry or liquid chromatography, this test can check for LF rapidly and with very high specificity and sensitivity.



Inventors: Anne Boyer, Conrad Quinn, John Barr
CDC Reference Number: I-013-06

Bordetella Pertussis

Diagnosis of *Bordetella Pertussis* (whooping) cough via Nucleic Acid Tests and Diagnostic Algorithm
This invention uses two nucleic acid targets in a polymerase chain reaction assay to better detect *Bordetella Pertussis* (whooping) cough. Currently available tests correctly diagnose *B. Pertussis* less than 20% of the time. They also fail to identify the causative agents of *B. Pertussis*, thereby missing cases preventable by current vaccination recommendations. The assay of this invention increases the diagnosis rate to over 70% and is able to differentiate between the three types of *Bordetella* infections, thereby distinguishing cases that are preventable by vaccination.

Inventors: Gary Sanden, Kai-Hui Wu, Leonard Mayer
CDC Reference Number: I-023-06

Chlamydia

Diagnostic Peptide Sequence Discovered for *Chlamydophilia pneumoniae*
Currently, there are few standardized assays for the detection of *Chlamydophilia pneumoniae* infection of humans. This invention is a peptide sequence that specifically binds *C. pneumoniae* and is recognized by anti-*C. pneumoniae* antibodies. This peptide may be useful for improving diagnostic methods by reducing the variability and high backgrounds found with methods that rely on whole organisms for detection. This peptide may also be useful for production of peptide or DNA vaccines.

Inventors: Eric Marston, Jackie Sampson, Stephen Skelton, George Carlone, Trudy Messmer
CDC Reference Number: I-016-00
Publication Number: WO02099039

Rapid Method for Molecular Differentiation of Chlamydia Trachomatis Biovars Strains
Infections caused by *Chlamydia trachomatis* are among the most prevalent sexually transmitted diseases in the United States. Infections may lead to pelvic inflammatory disease and infertility. Methods to identify and differentiate molecular types are critical for determining appropriate treatment. Currently, differentiation requires several days. This invention may differentiate *C. trachomatis* biovars in less than an hour while patients are waiting in the clinic.

Inventor: Hsi Liu

CDC Reference Number: I-003-03

Enterobacteriaceae

Oligonucleotide Probes for Detecting *Enterobacteriaceae* and Quinolone-Resistant *Enterobacteriaceae*

Enterobacteriaceae comprise *Salmonella, Shigella, Escherichia, Klebsiella, Enterobactor, Serratia, Proteus, Morganella, Providencia, Yersinia,* and several less common bacterial genera. These gram negative bacteria cause a wide variety of infectious illnesses. Specific oligonucleotide probes have been developed to be incorporated into methods for the species-specific identification of these *Enterobacteriaceae* in a sample as well as detection and diagnosis of *Enterobacteriaceae* infection in a subject. This invention further provides methods for species-specific identification of these quinolone-resistant *Enterobacteriaceae* as well as the detection and diagnosis thereof.

Inventors: Linda Weigel, Fred Tenover
CDC Reference Number: I-003-98
Patent Number: 6,706,475

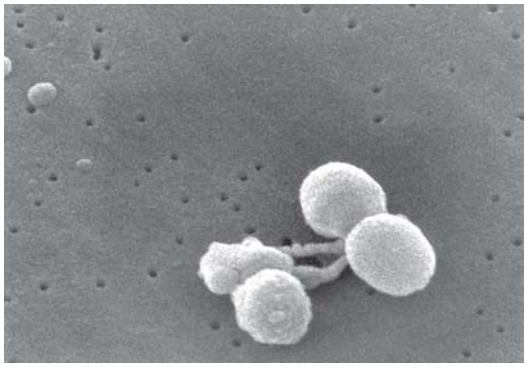
Mycoplasma pneumoniae

Development of Primers and Probe for Detection of *Mycoplasma pneumoniae* by Real-Time PCR

This real time PCR assay for detection of *Mycoplasma pneumoniae* has broad public health use for testing cases of unexplained respiratory illness, particularly in light of SARS epidemic concerns. The assay is useful in both clinical and research settings to study infections. *M. pneumoniae* is also associated with extrapulmonary infections which this assay can detect. The primers and probe have been successfully used on respiratory specimens; sputum; fresh, frozen and fixed tissues of all kinds; serum; whole blood; cerebrospinal fluid; and urine. The primers and probe were successfully tested for specificity against 100 other respiratory bacterial and viral pathogens, including other mycoplasma species which would be most likely to cross react. This assay is optimized to be run with the addition of an internal control (internal control covered under CDC Ref. I-036-03).

Inventors: Deborah Talkington, Mindy (Ming) Zang, Brian Holloway
CDC Reference Number: I-035-03

Highly Specific Primers and Probe for Detection *of Mycoplasma Pneumoniae* Infection



This invention involves a test for *Mycoplasma Pneumoniae* in a real-time PCR-based assay. Currently available assays require a large number of genome copies per sample as well as specific types of test samples that may not be available to the clinic. This CDC assay uses a specific primer sequence and fluorescent-tagged probe sequence to overcome these limitations, and can successfully detect *M. Pneumoniae* in respiratory specimens, sputum, tissues of all kinds, serum, whole blood, cerebrospinal fluids, and urine, and can do so with high specificity when as few as 1-5 genome copies per sample are present.

Inventors: Deborah Talkington, Mindy (Ming) Zhang, Brian P. Holloway
CDC Reference Number: I-017-06

Internal Controls and Control Probes for Identifying Inhibitors During Detection Assays of *Mycoplasma Pneumoniae* and *Mycoplasma Fermentans*

This invention covers DNA fragments and fluorescent-tagged probes used to evaluate the presence of inhibitors in PCR-based detection assays of *M. Pneumoniae* or *M. Fermentans*. The internal control probes bind specifically to the internal control DNAs and because of their fluorescence can be distinguished from PCR probes used in the same reaction. Current assays are limited by the required absence of inhibitors that prevent the polymerase in PCR assays from functioning. In the CDC's assay, the probes identify the presence of these inhibitors and thus detect false negative samples that would be reported in other assays.

Inventors: Deborah Talkington, Mindy (Ming) Zhang, Brian Holloway
CDC Reference Number: I-018-06

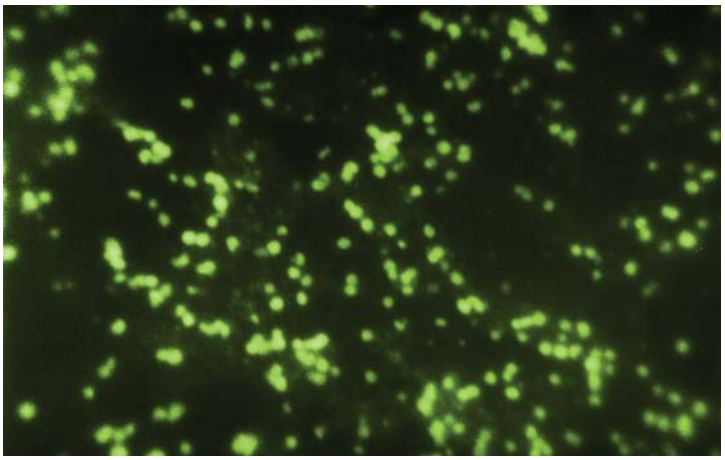
Neisseria meningitidis

Invasion Associated Genes from *Neisseria meningitidis* Serogroup B
The invention provides nucleic acids and encoded polypeptides associated with invasion of *Neisseria meningitidis*. The polypeptides are used as diagnostic reagents, as immunogenic reagents, and as components of vaccines. The nucleic acids are used as diagnostic reagents, as components of vectors and vaccines, and to encode the polypeptides of the invention. The invention also provides strains of *N. meningitidis* which have an invasion deficient phenotype.

Inventors: Fred Quinn, Nigel Raymond, Efrain Ribot, David Stephens
CDC Reference Number: I-002-95
Patent Number: 6,472,518

Nocardia farcinica

Rapid Identification of *Nocardia farcinica* by a PCR Assay
The bacterial complex *Nocardia* is a serious threat to immunosuppressed individuals, especially those with organ transplants, lung disease, and AIDS. *Nocardia farcinica* is the most clinically significant species because it characteristically demonstrates resistance to multiple, extended spectrum antimicrobial agents. Traditional identification methods are time consuming and labor-intensive (up to 8 weeks for definitive results). This invention comprises a unique DNA sequence within the *N. farcinica* genome which allows for PCR-based diagnostics which are specific to the species and do not cross react with closely related species and genera



Inventors: Brent Lasker, June Brown, Kim Pham
CDC Reference Number: I-027-00
Publication Number: 20050277136

Streptococcus pneumoniae

Development of Real-time PCR Assay for Detection of Pneumococcal DNA and Diagnosis of Pneumococcal Disease
An assay for detecting and diagnosing pneumococcal disease. It will provide a tool for quick and accurate diagnosis by clinicians, and for determining the efficacy of newly licensed polysaccharide-conjugate vaccines or future protein pneumococcal vaccines.

Inventors: Maria Da Gloria Carvalho, Jacquelyn Sampson, Edwin Ades, George Carlone, Richard Facklam, Karen McCaustland
CDC Reference Number: I-001-05

Peptide from *Streptococcus pneumoniae* Surface Adhesion A (PsaA) Protein Associated with Adherence
The peptide is a P4 peptide which contains functional epitopes of the PsaA protein of Streptococcus pneumoniae, and related methods and compositions. The technology also includes an antibody that can bind to the epitopes of the defined peptides. The technology is a complete kit that includes two vaccines comprised of two separate peptides, a pharmaceutical carrier for each vaccine, methods of using the peptides and antibodies, and diagnostic kits comprising a p4 peptide.

Inventors: Edwin Ades, Jacquelyn Sampson, Sandra Steiner, George Carlone, Joseph Caba, Gowrisankar Rajam
CDC Reference Number: I-030-04

Pneumococcal Fimbrial Protein A*
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes a pneumococcal fimbrial protein A suitable for vaccine and diagnostic purposes. In particular, the present invention describes polypeptides encoding a pneumococcal fimbrial protein A gene.

Inventors: Steven O'Connor, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91
Patent Number: 5,422,427

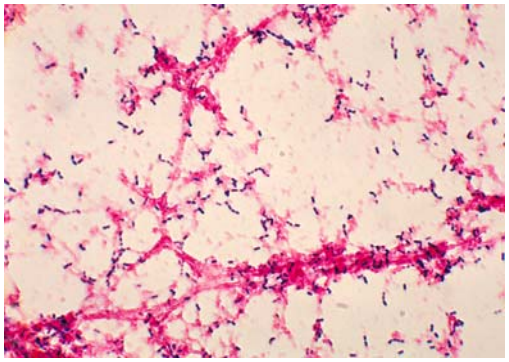
Pneumococcal Fimbrial Protein A*
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes nucleic acidsa encoding pneumococcal fimbrial protein A suitable for vaccine and diagnostic purposes.

Inventors: Steven O'Connor, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91
Patent Number: 6,312,944

Reduction in *Staphylococcus epidermidis* Viable Biofilm Formation on the Surface of a Hydrogel Coated Catheter Using *S. epidermidis* Bacteriophage PH456
The use of central venous catheters (CVCs) is often severely compromised as a result of bacterial biofilm formation. Bacteriophage therapy to reduce biofilm formation in CVCs has recently received renewed interest as a possible alternative for the treatment of infection. Initially a model of S. epidermidis 414 biofilm formation on hydrogel coated silicone catheter segments was developed in a modified Drip Flow Biofilm Reactor. Heat inactivated bacteriophage resulted in a reduction of *S. epidermidis* catheter associated biofilm formation. Thus, in-vitro data supports the potential value of bacteriophage impregnated catheter surfaces for reducing infection.

Inventors: John Curtin, Rodney Donlan
CDC Reference Number: I-003-05

Hydrogel-bacteriophage Coating for the Reduction/Prevention of Biofilm Formation on Biomedical Implants
Inventor: John Curtin
CDC Reference Number: I-009-04



Streptococcus pneumoniae* 37-kDa Surface Adhesin A Protein
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes a pneumococcal protein suitable for vaccine and diagnostic purposes. This invention includes an isolated nucleic acid encoding the 37-kDa protein of *S. pneumoniae* surface adhesin A, and unique fragments of the nucleic acid encoding the 37-kDa protein of *S. pneumoniae* surface adhesin A.

Inventors: George Carlone, Jacqueline Sampson, Harold Russell
CDC Reference Number: E-157-91
Patent Number: 5,854,416

Streptococcus pneumoniae* 37-kDa Surface Adhesin A Protein and Nucleic Acids Coding Therefore
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. This invention includes a pneumococcal protein suitable for vaccine and diagnostic purposes. This invention includes methods of vaccination using unique the 37-kDa protein of *S. pneumoniae* surface adhesin A.

Inventors: Jacqueline Sampson, Jean Tharpe, Harold Russell, Edwin Ades, George Carlone
CDC Reference Number: E-157-91
Patent Number: 6,217,884

Recombinant Lipidated PsaA Protein, Methods of Preparation and Use*
Disease caused by Streptococcus pneumoniae (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is very prevalent among the very young, the elderly, and immunocompromised persons. The present invention relates to recombinant lipidated PsaA proteins and recombinant

constructs from which such lipidated PsaA proteins may be expressed. The invention also provides methods of preparation of lipidated PsaA proteins and use of such proteins in immunological compositions. Also provided are vaccines comprising immunogenic lipidated PsaA proteins and methods of use of such vaccines in the prevention and treatment of S. pneumoniae infection.

Inventors: Barun De, Robert Huebner, Jacqueline Sampson, Edwin Ades, George Carlone
CDC Reference Number: I-011-97
Publication Number: WO9940200

Methods and Compositions for the Simultaneous Detection of Multiple Analytes
Epidemiological and vaccine studies of *Streptococcus pneumoniae* and *Chlamydia* require serotype identification. Current methods of serotyping are labor intensive and subjective. This invention utilizes serotype specific antibodies bound to fluorescent beads which allows for simultaneous single tube capture and detection of all *S. pneumoniae* serotypes and three *Chlamydia* serotypes.

Inventors: Melinda Bronsdon, George Carlone, Joseph Martinez
CDC Reference Number: I-009-99
Publication Number: WO9945121

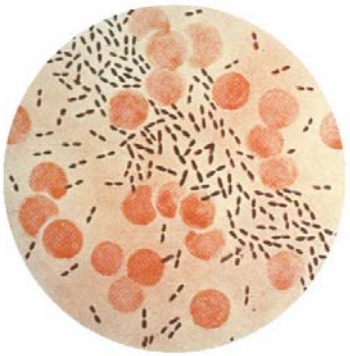
Oligonucleotide Sequences for Amplification of *Streptococcus pneumoniae* Gene
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. The present invention relates to diagnostic assays and kits for detecting the presence of *S. pneumoniae* in a sample and to vaccines for use against *S. pneumoniae*. More specifically, the invention relates to PCR assays for the presence of *S. pneumoniae* surface adhesion A protein (PsaA) and to vaccines raised against a portion of PsaA encoded by a PCR product that is provided using specific primers.

Inventors: Edwin Ades, Jennifer Crook, Jacqueline Sampson, George Carlone, Katherine Morrison
CDC Reference Number: I-013-99
Patent Number: 6,869,767

Multiple Antigenic Peptides Immunogenic against *Streptococcus pneumoniae*
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. This invention is an improved peptide construct consisting of a combination of antigenic epitopes of the PsaA (37-kDa) protein from *Streptococcus pneumoniae*. This construct is a possible vaccine candidate which may provide better immune stimulation over vaccines which are based on individual rather than combination epitopes.

Inventors: Danny Jue, Jacqueline Sampson, Scott Johnson, George Carlone, Edwin Ades
CDC Reference Number: I-014-00
Patent Number: 6,903,184

Epitope Peptides Immunogenic against *Streptococcus pneumoniae*
Disease caused by *Streptococcus pneumoniae* (pneumococcus) is an important cause of morbidity and mortality in the United States and developing countries. Pneumococcal disease is prevalent among the very young, the elderly, and immunocompromised persons. This invention describes novel immunogenic peptides obtained from a random library by selection for high affinity binding to monoclonal antibodies specific for PsaA epitopes. In addition, the peptides of the invention have the capability of serving as immunogens in a subject, thereby effectively eliciting the production of antibodies by the subject and additionally conferring protective immunity against infection by *S. pneumoniae*.



Inventors: George Carlone, Maria Westerink, Edwin Ades, Jean Tharpe, Joan Zeiler, Jacqueline Sampson
CDC Reference Number: I-017-97
Publication Number: WO9945121

Multiplexed Pneumococcal Serotyping Assay
This invention comprises a multiplexed screening assay capable of accurately identifying 85-90% of *Pneumococci* serotypes causing disease in the U.S. This assay identifies specific capsular polysaccharides unique to each serotype and provides public health workers with information used for vaccine design, vaccine responses, and trends in pneumococcal disease.

Inventors: Joseph Martinez, George Carlone, Bernard Beall, Terry Thompson
CDC Reference Number: I-001-06

Group A Streptococci

Peptide Vaccines against Group A Streptococci
This invention relates to synthetic Group A streptococci (GAS) immunoreactive peptides, compositions comprising the peptide sequences, vaccines, isolated antibodies elicited by the peptides, diagnostic kits comprising the peptides or antibodies, and methods of using the peptides, compositions, vaccines and antibodies. The synthetic peptides of the invention are immunoreactive portions of the M proteins of the most prevalent GAS serotypes in the United States

Inventors: Bernard Beall, George Carlone, Edwin Ades, Jacqueline Sampson
CDC Reference Number: I-039-00
Publication Number: WO02094851

MISCELLANEOUS and METHODOLOGIES

Cell Line

Immortalized Endothelial Cell Line
Endothelial cells are critical components of wound healing, inflammation, circulation, and tumor growth metastases. Endothelial cells are difficult to isolate and culture. A unique approach has been used to immortalize endothelial cells, which are more amenable to culture. The cell line, designated HMEC-1, provides a ready source of human endothelial cells for research, including studies on the physiologic and pathologic factors that induce endothelial mitosis, pharmacological studies for the screening of various agents, and toxicological studies for the cosmetic and pharmaceutical industry.

Inventors: Edwin Ades, Francisco Candal, Thomas Lawley
CDC Reference Number: E-036-91

Medical Device

Method and Apparatus for Cough Sound Analysis
Lung diseases can be differentiated by the location of effect in the lungs which produce variations in cough sounds and patterns. This invention allows subjects to cough into a tubing system allowing the acoustics generated to be recorded with high fidelity and transferred to a computer. Based on these differences, analysis software estimates the lung disease type of the subject. Those who benefit from cough sound analysis include subjects in the early stages of undetected lung disease, subjects with conditions not easily diagnosed by standard techniques, subjects who demonstrate difficulty performing forced expiratory maneuvers and other pulmonary function tests (e.g., elderly, young, and very sick patients), and workers whose respiratory functioning may change during the workday.

Inventors: Walter McKinney, Jeffrey Reynolds, David Frazer, Travis Goldsmith, Aliakbar Afshari, Kimberly Friend
CDC Reference Number: I-020-99
Patent Number: 6,436,057

Mixing Vial
Current vaccine technologies require reconstitution of lyophilized vaccines by drawing sterile diluent from a sealed vial via needle and syringe and injecting it into another sealed vial containing the lyophilized vaccine. The need for two vials gives the possibility of contaminating the vaccine in the reconstitution process, using the wrong diluent (which has been fatal in rare cases), or the wrong amount of diluent and the possibility of needle stick injuries. The two vial system requires more materials, more labeling and more storage space. This invention is a single reconstitution system in which both the lyophilate and the diluent are contained in a single vial. In addition to resolving the above difficulties, with the single vial system the diluent is refrigerated along with the lyophilate and provides a thermal buffer to keep the lyophilate temperature stable.

Inventors: Mark J Papania, Mark C Bagley, James J Barry
CDC Reference Number: I-005-02
Publication Number: WO2004000678

Auscultatory Training System
This auscultatory training apparatus includes a database of prerecorded physiological sounds (e.g., lung, bowel, or heart sounds) stored on a computer for playback. The program allows a user to select prerecorded sounds for playback. In addition, the program is operable to generate an inverse model of the playback system in the form of a digital filter. The inverse model processes the selected sound to cancel the distortions of the playback system so that the sound is accurately reproduced. The program also permits the extraction of a specific sound component from a prerecorded sound so that only the extracted sound component is audible during playback. As well as a teaching tool to instruct the user on various body sounds, this invention could have applications as a diagnostic screening tool and as a telemedicine tool.

Inventors: Walter McKinney, Jeffrey Reynolds, Travis Goldsmith, Kimberly Friend, David Frazer
CDC Reference Number: I-037-00
Publication Number: 20020183874

Medical Software

A Video-Synchronized Multi-Channel Biomedical Data Acquisition System
New biomedical devices often require the acquisition of data in multiple forms which must be synchronized for analysis. This data acquisition system, modeled on methods used for muscle fatigue analysis, synchronizes images captured on video tape with digital data acquired on computer disk.

Inventors: Hongwei Hsiao, Shengke Zeng, John Powers
CDC Reference Number: I-001-99
Publication Number: WO0127855

Automated Microscopic Image Acquisition, Compositing, and Display
Micro-Screen is a software program designed to capture images, archive, and display a compiled image(s) from a portion of a microscope slide in real time. This program allows for the recreation of larger images which are constructed from individual microscopic fields captured in up to five focal planes and two magnifications. This program may be especially useful for the creation of data archives for diagnostic and teaching purposes and for tracking histological changes during disease progression.

Inventors: Maribeth Gagnon, Richard Draut, Ed Kurjawski, Roger Taylor, James Lang, Tommy Lee, Carlyn Collins
CDC Reference Number: I-019-00

Finding Usable Portion of Sigmoid Curve
Sigmoid curves are commonly generated in bioassays and used to calculate results. Various techniques have been used to define the curve, analyze the observations, and calculate a concentration. This technology is an algorithmic approach to identifying the usable portion of a sigmoid. . This approach is more objective than other methods, reducing the variability introduced by individuals and/or by repetition and allows substantially higher throughput in a situation where a lot of samples are being analyzed using the same assay.

Inventor: Thomas Taylor
CDC Reference Number: I-019-02
Publication Number: WO2004084708

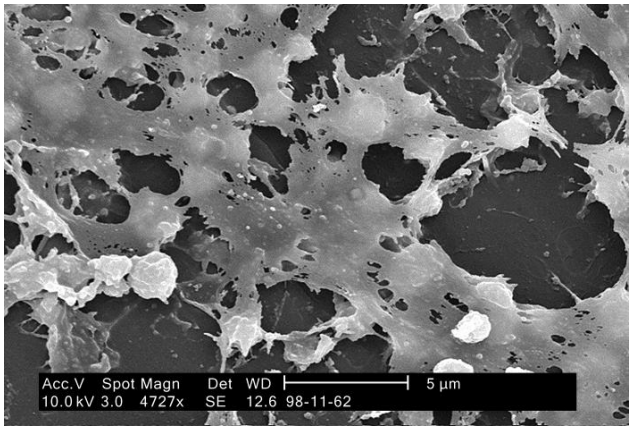
Organ Culture

Artificial Organ Culture System
An artificial organ system comprising an artificial microporous membrane with a confluent layer of endothelial cells on one side and a confluent layer of epithelial cells on the other side has been provided. The organ system provided is contained in a vessel. A method for constructing the artificial organ system is also provided. The artificial organ system may be used for studying endothelial passage of pathogens and chemical substances.

Inventors: Fred Quinn, Kristin Birkness, Edwin Ades

CDC Reference Number: E-121-94
Patent Number: 5,695,996

Microbial Biofilm



Multicoupon Biofilm CFSTR
This device will allow the study of methods to control microbial biofilm formation. The apparatus is used to grow microbial biofilms on multiple, removable substrata for the purpose of determining the effect of selected variables including material of construction, growth medium, and antimicrobial agent concentration, on the growth and activity of biofilm-associated microorganisms.

Inventors: Ricardo Murga, Rodney Donlan, Douglas (Wayne) Kirby
CDC Reference Number: I-006-01

Miscellaneous

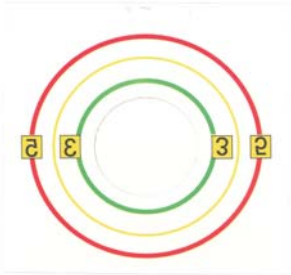
Artificial Human Mutation Controls for Diagnostic Testing
Molecular genetic test development, validation, quality control (QC), quality assurance (QA), and required proficiency testing have historically been hampered by a lack of sufficient positive control material, which generally has been dependent on patient samples donated by laboratories. These samples are often scarce, if available at all, for some genetic tests. The inventors propose a method for synthesizing positive control samples for any genetic disorder for which the coding sequence is known. These are combined with background material in a proprietary formulation to accurately mimic actual samples from patients with the disorder of interest. The technique applied allows for the creation of a permanently transformed control sample with realistic dosing, that accurately mimics the performance of actual patient samples in molecular genetic testing. This technique will enable the synthesis of positive control materials for many molecular genetic tests, and is likely to lead to the development of positive control samples for molecular screening of oncogenes and non-infectious controls for infectious disease testing.

Inventors: Laurina Williams, Wayne Grody, Ramaswamy Iyer, Michael Jarvis
CDC Reference Number: I-007-04
Publication Number: WO2005086938

Device to Measure Muscle Contractile/Relaxant and Epithelial Bioelectric Responses of Perfused, Intact Airways *In Vitro*
Allows, for the first time, measurement of smooth muscle contractile/relaxant activity and transepithelial potential difference (Vt) [or short circuit currents (Isc)] and resistance (Rt) simultaneously in an intact airway in vitro. Investigation of the mechanisms of lung diseases, such as asthma and cystic fibrosis, involves understanding the roles of the airway smooth muscle and epithelium. The smooth muscle is involved in the control of the airway diameter; the epithelium regulates the ionic composition of the liquid lining the airways through electrogenic ion transport and it releases factors that regulate the ability of smooth muscle to contract. The present invention allows simultaneous measurement of smooth muscle contractile/relaxant activity, Vt and Rt under conditions in which the normal spatial relationships between all the cell types are retained and the airway wall is not surgically manipulated or distorted. Because agents can be added separately to the lumen, where they must first cross the epithelium to reach the smooth muscle, or to the outside of the airway, where there is no hindrance of agents to the muscle, the device permits evaluation of functional integrity of the epithelium using pharmacological techniques. It also will permit the effective screening of the effects of agents and drugs on airway epithelium and smooth muscle in the same preparation

Inventors: Jeffrey Fedan, Yi Jing, Michael Van Scott
CDC Reference Number: I-004-05

Method for Monitoring Local Reaction Associated with Injections
A simple and inexpensive method to give patients a guideline for determining the severity of an adverse reaction that may occur at the site of injection. Patients can be instructed to notify health care providers if an inflammatory response spreads beyond a measured distance from the location of injection.



Inventors: Laurie Kamimoto

CDC Reference Number: I-036-00
Patent Number: 6,833,128

Method for Retaining Methylation Pattern in Globally Amplified DNA
A novel method that results in globally amplified DNA copies that retain the methylation signature to make a DNA archive for methylation studies (Meth-DNA archive). Rather than assaying BST-DNA directly by PCR or by sequencing methods, a portion is subjected to multiple strand displacement amplification (MDA) using Phi 29 DNA polymerase (Fig. 1). MDA results in bisulfite treated globally amplified DNA (Meth-DNA) retaining the methylation signature present in the original DNA. Aliquots of Meth-DNA archive are used in assays similar to those designed for BST-DNA to indicate methylation status of cytosines such as pyrosequencing, methylation specific PCR, or dideoxy sequencing. A Meth-DNA archive is thus created for large scale methylation studies by employing MDA on bisulfite treated DNA. The novel method described here for creating a Meth-DNA archive should eliminate a significant bottleneck in the collection of methylation information in the genomes of host and pathogens, and thus provide numerous opportunities for the early detection, control and prevention of many chronic and infectious diseases of public health importance.

Inventors: Mangalathu Rajeevan, Elizabeth Unger
CDC Reference Number: I-019-05

PCR Exchangeable Template Reaction
There exists a great need for an efficient means to make synthetic DNA of any desired sequence. Such a method could be universally applied. For example, the method could be used to efficiently make an array of DNA having specific substitutions in a known sequence which are expressed and screened for improved function. The present invention satisfies these needs by providing an efficient and powerful method for the synthesis of DNA. The method is generally referred to as the Exchangeable Template Reaction (ETR) which provides for the synthesis of DNA based on a cyclic mechanism of combining deoxyoligonucleotides. Also included is a series of unique synthesized single-stranded deoxypolynucleotides which can be enzymatically treated to form a unique 3' single-stranded protrusion for selective cyclic hybridization with another unique single-stranded deoxypolynucleotide of the series.

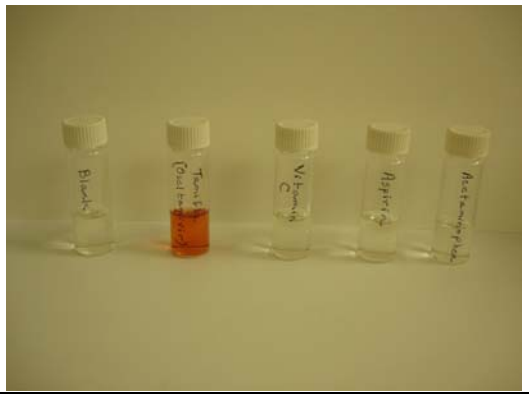
Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: E-184-91
Patent Number: 5,503,995

Methods for the Prevention and Treatment of Diseases Caused by an Inflammatory Response
This invention provides methods for preventing or treating a disease in a subject caused by an inflammatory response to a disease or syndrome that is mediated by endogenous substance P. The methods include administration of anti-substance P antibodies or anti-substance P antibody fragments.

Inventor: Ralph Tripp
CDC Reference Number: I-009-98
Publication Number: WO0043040

Method for Detecting Counterfeit Drugs
Artemisinin and artemisinin derivatives (e.g., artemether, artesunate, and dihydroartemisinin) are used in antimalarial drugs. The widespread emergence of counterfeit drugs has led to the death of many patients who would have survived if given the genuine drug. The illicit trade in fake antimalarials is a serious economic and public health problem. This kit is a relatively easy to use and inexpensive test to detect fake antimalarial tablets and confirm the authenticity of artemisinin and derivative drugs.

Inventor: Michael D Green
CDC Reference Number: I-008-01
Publication Number: WO03048766



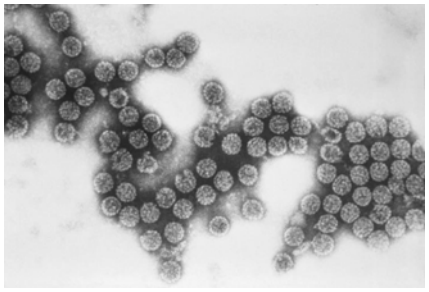
Method for Testing Authenticity of Tamiflu (Oseltamivir)
This invention describes a method to test the authenticity of Tamiflu (Oseltamivir) medication. Because of the popularity and continued effectiveness of this medication in conjunction with the recent outbreaks of avian flu, criminal elements have begun producing and distributing counterfeit versions of Tamiflu to sell to unsuspecting consumers. This invention would provide a simple color-based test for determining a

drug's authenticity that could be administered on site by Customs or Border Protection officers and would be a valuable tool in the fight against counterfeit drugs.

Inventor: Michael Green
CDC Reference Number: I-024-06

In-Tube Method and Apparatus for Blood Stimulation and Plasma Collection
Measurement of biological responses that occur when blood is stimulated with various antigens can provide important information about disease and risk of disease. However, the current methods used to measure the responses are not only complicated but laborious. Because of the complexity of the process it is extremely susceptible to human error. The assays can be simplified and made easier by collecting blood directly into a tube that already contains the antigen, and that has a gel plug in the bottom. After collecting the blood and mixing it with the antigen in the tube, the tube is incubated overnight. After incubation, the tube is spun to separate cells from the plasma. This allows for easy collection and automation of the stimulation process.

Inventor: Gerald "Jerry" Mazurek
CDC Reference Number: I-022-04



Use of Cyanidin-3-Glucoside as an Anti-Tumor Treatment
Cyanidin 3 glucoside inhibits neoplastic transformation, metastasis, neoplastic cell migration and invasion, and activation of NF êB, AP 1, COX 2, TNF á and MAPK, and induces apoptosis in neoplastic cell (such as HL 60 cells). Cyanidin 3 glucoside is also demonstrated to possess strong antioxidant activity involving, at least, inhibition reactive oxygen species and induction of cytoprotective genes.

Inventor: Min Ding
CDC Reference Number: I-023-04

Rapid Method for Detecting Cardiovascular Disease
With this invention a cardiovascular disease profile may be obtained in as little as 2-3 hours. These chips can be used in doctors' offices and ambulances in conjunction with other currently used clinical techniques such as those reported by Dayal and Ertel to rapidly detect and identify apolipoproteins, thus giving the earliest possible warning of cardiovascular disease. This invention covers a rapid apolipoprotein fingerprinting method useful for identifying and measuring CI (CI-1, CI-2), CII, CIII ($C111_0$, $C111_1$, $C111_2$), and other low density proteins in order to detect cardiovascular disease. With the appropriate antibodies, this invention can detect multiple apolipoproteins simultaneously; directly in human plasma or serum; and without the need for ultracentrifugation, electrophoresis, or delipidation. This technique applies serum or plasma samples directly to surface-enhanced chips coated with Protein G and purified antibody mixtures, causing the aforementioned apolipoproteins to bind to the surface. They can then be measured using laser desorption ionization time-of-flight mass spectrometry to provide an enhanced apolipoprotein profile.

Inventors: Mary Robinson, Emelita Breyer, Kirtan Koticha, Arron Xu
CDC Reference Number: I-015-06

Microarray

PNI Microarray and Uses
Due to the complexity of interactions between immune, endocrine, and nervous systems, assays for one or a few biomolecular markers can be uninformative or misleading. Accordingly, diseases which are characterized by disturbances in one or more of these systems, and the interactions between them, are among our most significant research and clinical challenges. This oligonucleotide microarray is composed entirely of PsychoNeuroendocrine-Immune (PNI) genes which will allow a researcher to assess the overall PsychoNeuroendocrine-Immune state of an individual, and to observe systemic responses.

Inventors: Ainsley Nicholson, Suzanne Vernon
CDC Reference Number: I-011-03
Publication Number: WO2004108899

Integration of Gene Expression Data and Non-Gene Data
Over the last decade, advances in microarray technologies have made gene expression studies increasingly reliable and accessible. These developments have dramatically enhanced the potential for complex gene expression analysis. This invention

provides the ability to integrate gene expression data with epidemiologic data. Such analyses can assist in providing diagnostic and prognostic information and profiling disease susceptibility.

Inventors: Suzanne Vernon, Elizabeth Unger, William Reeves, Dan Bui, Stanley Lucas, Amarendra Yavatkar
CDC Reference Number: I-024-02
Publication Number: WO2004050840

Microscope

Improved Compression Algorithm for Images in a Focal Stack
This invention offers a superior method to those currently available for the compression of focal stack images. A focal stack of images is a collection of consecutively focused images from a microscope. Normally, images are compressed individually; this invention takes advantage of the knowledge that images are collection of focal planes to improve compression.

Inventors: Maribeth Gagnon, Ed Kujawski
CDC Reference Number: I-016-06

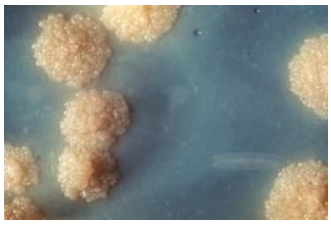
Improved Image Acquisition for Bright Field Microscopy
This invention improves the quality of images captured from a bright field microscope using a collection of captured images at different shutter speeds. The technology provides the ability to form a composite image that mimics the image viewed by the human eye.

Inventors: Maribeth Gagnon, Ed Kujawski
CDC Reference Number: I-020-06

MYCOBACTERIAL

Tuberculosis

SecA Gene of *Mycobacterium tuberculosis* and Related Methods and Compositions
Tuberculosis is a mycobacterial disease which is a major cause of disability and death in the developing world and immunocompromised patients. This invention includes an isolated nucleic acid encoding a SecA protein of *Mycobacteria tuberculosis* and provides methods of screening for putative *M. tuberculosis* virulence factors translocated by the SecA protein. These may further provide for useful vaccines and diagnostic tests for active tuberculosis.



Inventors: Michael Schmidt, Fred Quinn, Marie Owens, Harold King
CDC Reference Number: E-066-95
Patent Number: 5,885,828

A Method for the Rapid Diagnosis of Infectious Disease by Detection and Quantification of Microorganism Induced Cytokines
This invention covers a new method to rapidly and easily detect and quantify cytokines in a patient's blood. Currently available *in vitro* methods to detect latent *Mycobacteria tuberculosis* and other infectious diseases are laborious and expensive because they rely on measuring interferon-gamma response in patient's blood cells. CDC's technology, on the other hand, test detects interferon-gamma and other cytokines using the inherent properties of these molecules in a competitive assay. CDC's new detection method is simpler and easier to perform, thereby rendering new *in vitro* methods faster and less expensive.

Inventors: Gerald "Jerry" Mazurek, Malford E. Cullum
CDC Reference Number: I-038-04
Publication Number: 20050164168

Antibiotics Against Resistant Strains of *M. Tuberculosis* and Methods for Producing Them
This invention may be used to produce cyclic peptide antibiotics effective against newly discovered, resistant strains of *M. Tuberculosis*. These new strains of *M. Tuberculosis* have an inactivated tlyA gene and show resistance to currently available treatments, including capreomycin and viomycin. This previously uncharacterized tlyA gene was found to modify a cytidine on each ribosomal subunit of the mycobacterium and may be responsible for this resistance.

Inventors: Bonnie Plikaytis, Gilles Van Wezel, Stephen Douthwaite, Courtney Maus

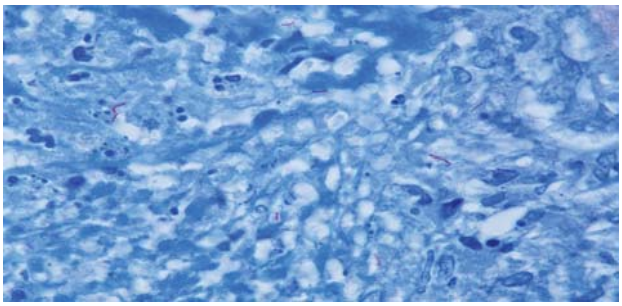
CDC Reference Number: I-014-06

MYCOTIC

Aspergillus

Development of DNA Probes to Identify *Aspergillus* Species
This invention provides specific DNA (oligonucleotide) probes and methods needed to identify *Aspergillus versicolor* and *Aspergillus ustus* and to differentiate these *Aspergillus* species from other medically important fungi. The invention includes a control probe plate to insure run-to-run reproducibility.

Inventors: Christine Morrison, Steven Hurst, Hans Hinrikson
CDC Reference Number: I-008-04



The Production of Cross-Reactive Monoclonal Antibodies Against *Aspergillus* and *Penicillium* Species
Monoclonal antibodies raised against *Aspergillus versicolor*. These antibodies are not species specific and cross react against multiple *Aspergillus* species and *Penicillium* species.

Inventors: Detlef Schmechel, Daniel Lewis
CDC Reference Number: I-022-03

Detection

Development of DNA Probes to Detect Fungal Pathogens Using a Multi-Analyte Profiling System
Specific DNA probes were developed to identify *Candida* species and endemic mycoses and to differentiate them from other medically important fungi in a multi-analyte profiling system. This system can simultaneously identify up to six different fungi in a single sample and has the potential to identify up to 100 different fungi at once. This method would provide a very rapid and specific diagnosis allowing the administration of appropriate antifungal drug therapy.

Inventors: Christine Morrison, Sanchita Das, Teresa Brown, Brian Holloway
CDC Reference Number: I-022-05

Histoplasma capsulatum

Nucleic Acids of the M Antigen Gene of *Histoplasma*, Isolated and Recombinant-Produced Antigens, Vaccines and Antibodies, Methods and Kits for Detecting Histoplasmosis
Histoplasmosis is a mycotic infection of varying severity, usually localized in the lungs. Caused by *Histoplasma capsulatum*, infections are usually symptomatic but can develop into chronic disease, especially in immune compromised individuals. The present invention relates to reagents and methods for the detection of histoplasmosis. In particular, the present invention relates to nucleic acids (DNAs) relating to the M antigen gene of *Histoplasma capsulatum*; to vectors and host expression systems containing these nucleic acids; to nucleic acids (RNAs) which encode the M antigen of *H. capsulatum*; to isolated and recombinant-produced antigens encoded by these nucleic acids; to antibodies produced against these antigens; to methods and kits for detecting histoplasmosis using these nucleic acids, antigens and antibodies; and to vaccines for the treatment of prevention histoplasmosis.

Inventors: Timothy Lott, Errol Reiss, Rosely Zancope-Oliveira, George Deepe, Leonard Mayer
CDC Reference Number: I-002-97
Publication Number: WO9955874

Rapid and Sensitive Method for Detecting *Histoplasma capsulatum*
Histoplasmosis is a mycotic infection of varying severity, usually localized in the lungs. Caused by *Histoplasma capsulatum*, infections are usually symptomatic but can develop into chronic disease, especially in immune compromised individuals. This invention relates to detecting *Histoplasma capsulatum* by PCR using oligonucleotide probes specific for *H. capsulatum*. Test samples may originate from the environment, where *H. capsulatum* spores are found or from clinical samples obtained from patients. Furthermore, the invention also provides for methods that detect the presence of *H. capsulatum* in a sample using a nested, or two-stage, PCR assay.

Inventors: Millie Schafer, Thomas Reid
CDC Reference Number: I-006-97
Patent Number: 6,469,156

Stachybotrys chartarum

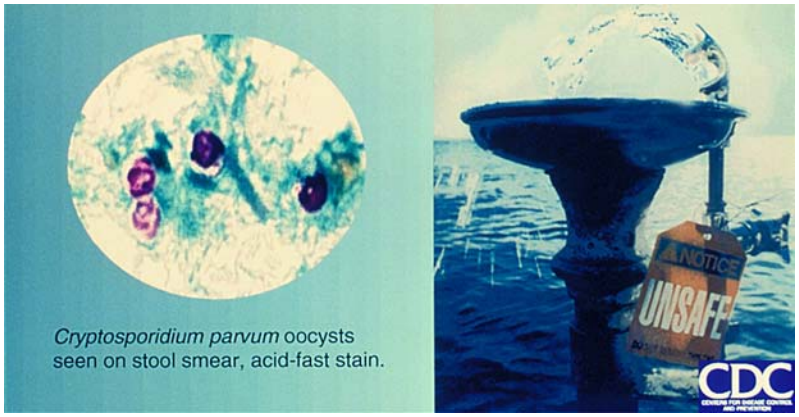
Monoclonal Antibodies against Fungi and Methods for Their Use
Certain fungi found in indoor environments, including homes and businesses, may cause adverse health effects in people and animals by causing infection or provoking allergic reactions. Sick building syndrome, an occupational condition in which workers are sickened by environmental toxins or pathogens, has been associated with the fungus *Stachybotrys chartarum*. This invention provides monoclonal antibodies that can be used to rapidly and accurately test for the presence of fungi in the environment. These antibodies may also be used to assess human exposure to fungi by testing blood and other bodily specimens.

Inventors: Detlef Schmechel, Daniel Lewis
CDC Reference Number: I-002-01
Publication Number: WO03016352

PARASITIC

Cryptosporidium parvum

Methods for Detecting *Cryptosporidium parvum* Oocysts
This invention includes methods for detecting parasites, such as *Cryptosporidium parvum*, in turbid and non-turbid samples by solubilizing molecular markers or antigens of the parasite. The molecular markers are solubilized by incubating a sample containing the parasite with a solubilization buffer and detecting the solubilized antigens by electrochemiluminescence. The solubilization buffer contains one or more detergents alone or in combination with one or more denaturing agents in a buffered solution. The methods are an improvement over existing immunofluorescence assays for *C. parvum* because the methods described therein are quantitative, reproducible, have high sensitivity, are not labor-intensive, require only minimal sample processing, and avoid being adversely affected by sample turbidity. In addition, by using an electrochemiluminescence assay, microscopy is not required.



Inventors: Michael Arrowood, Yeuk-Mui Lee, Victor Tsang, Jeffrey Call, Patrick Johnson
CDC Reference Number: I-010-97
Patent Number: 6,475,747

Reagent and Method for Detecting *Cryptosporidium parvum* Oocysts
Cryptosporidium parvum is a parasite which can cause severe diarrhea. It is often spread through contaminated drinking water and unpasteurized juices. Provided are a reagent and method for the specific and highly sensitive detection of *C. parvum* in which the regent is an antibody for a soluble *C. parvum* sporozoite antigen. The assay allows recognition and detection of *C. parvum* in turbid samples. Since there is a lack of crossreactivity with other *Cryptosporidium* species, the assay is also highly specific for *C. parvum* contamination or infection.

Inventors: Long-Ti Xie, Victor Tsang, Kathy Hancock, Jeffrey Call, Michael Arrowood, Yeuk-Mui Lee, Patrick Johnson
CDC Reference Number: I-039-98
Publication Number: WO0033873

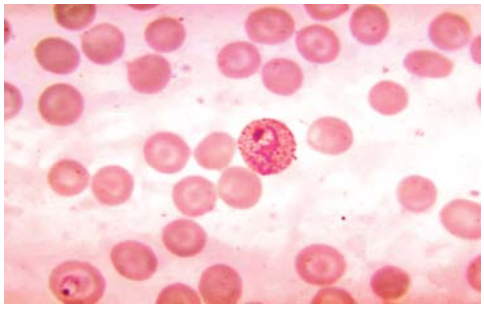
Malaria

Compositions and Methods for Inhibiting Transmission of Malaria
Current malaria vaccine development efforts focus primarily on moderating infection in the human host rather than targeting the mosquito vectors responsible for the spread of malaria. A set of monoclonal antibodies has been developed which inhibit

the development of human malaria parasites in different species of mosquitoes by blocking specific mosquito antigens. It may be possible to develop a malaria transmission blocking vaccine by immunizing humans with DNA or protein forms of the identified mosquito antigens. The human antibodies elicited against such antigens, when ingested by the mosquito along with infectious parasites, may prevent the development of parasites in the mosquito and thus halt malaria transmission.

Inventors: Altaf Lal, Pamela Patterson
CDC Reference Number: I-002-00
Publication Number: WO0211757

An Improved Recombinant Multivalent Malarial Vaccine Against *Plasmodium Falciparum*



The chimeric immunogenic polypeptides comprise peptide eptitopes derived from different stages in the life cycle of the malarial parasite, and, in particular, the *Plasmodium falciparum* parasite. In some embodiments, spacer amino acid sequences are inserted between epitopes. The disclosed chimeric immunogenic polypeptides can be used to stimulate an immune response to the *P. falciparum* parasite in a subject.

Inventors: Altaf Lal, Lihua Xiao, Charles Todd, Paul Schnake, Zhiyong Zhou, Ya Ping Shi, Robert Wohlhueter, Venkatachal Udhayakumar
CDC Reference Number: I-019-03
Publication Number: WO2006019427

Recombinant Multivalent Malarial Vaccine against *Plasmodium falciparum*

Malaria continues to be a public health problem throughout the world. *Plasmodium falciparum* is often identified as the cause of the most severe forms of malaria. This invention relates generally to the development and use of a recombinant, multi-valent and multi-stage malaria vaccine and more specifically relates to an antigenic protein useful for preventing or treating *P. falciparum* malarial infections. The invention further provides a vaccine against malaria that is effective in inhibiting reproductive growth of the parasite within a human or animal after initial infection. Also, this invention provides a method for conferring immunity against different stages in the life cycle of the malarial parasite, *P. falciparum*. Furthermore, the invention includes antibodies against a recombinant protein containing antigenic epitopes to various stages of a malarial *Plasmodium* species that may be useful as research or diagnostic reagents for the detection and measurement of *P. falciparum* in a biological sample.

Inventors: Ya Ping Shi, Altaf Lal, Seyed Hasnain
CDC Reference Number: I-004-98
Patent Number: 6,828,416

Taenia solium

Isolation of Diagnostic Glycoproteins to *Taenia solium*, Immunoblot-Assay and Method for the Detection of Human Cysticercosis

Human cysticercosis is a potentially fatal invasion of various tissues by the larvae of *Taenia solium*. The disease has increased dramatically in prominence as a medical problem in the United States since 1977. Increased travel and immigration from highly endemic areas such as Mexico and Central America make recognition and treatment of cysticercosis a U.S. public health priority. This invention is a method and a kit for diagnosing active human neurocysticercosis utilizing an immunoblot assay. This method allows diagnosis of neurocysticercosis by the detection of antigens of larval origin and improves on the specificity and sensitivity of the disc method, achieving 98% sensitivity and 100% specificity. This kit also allows the detection of antibodies in the serum or cerebrospinal fluid.

Inventors: Joy Brand, Anne Boyer, Marianna Wilson, Shirley Maddison, Victor Tsang, Peter Schantz
CDC Reference Number: E-185-88
Patent Number: 5,354,660

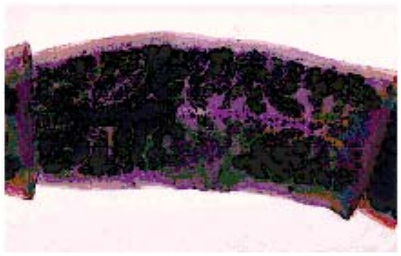
Compositions and Methods for Detecting Adult *Taenia solium*

Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasis. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is

itself not dangerous, cysticercosis can be fatal. This invention describes adult *T. solium* polypeptides which can be useful as diagnostic agents for the detection of adult tapeworm infection.

Inventors: James Allan, Victor Tsang, Patricia Wilkins
CDC Reference Number: I-028-97
Patent Number: 6,379,906

Methods and Compositions for Detecting Larval Taenia solium with a Cloned Diagnostic Antigen
Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasisis and is acquired by ingestion of *T. solium* cysticerci found in raw and undercooked pork muscle or food contaminated with human or pig feces. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is itself not dangerous, cysticercosis can be fatal. In the present invention, the gp50 antigen has been cloned and may be useful for improvements over the existing Western blot diagnostic method for identifying individuals with cysticercosis.



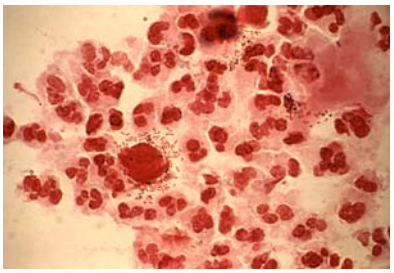
Inventors: Kathy Hancock, Ryan Greene, Victor Tsang, Patricia Wilkins
CDC Reference Number: I-031-99
Publication Number: WO01754448

T24 Antigen for Immunodiagnosis of Taenia Solium Cysticercosis
Taenia solium is a species of tapeworm. Intestinal infection with it is referred to as taeniasis. Many infections are symptomatic but may be characterized by insomnia, anorexia, abdominal pain and weight loss. Cysticercosis is the formation of cysticerci in various body tissue resulting from the migration of the *T. solium* larvae out of the intestine. Although infection with *T. solium* is itself not dangerous, cysticercosis can be fatal. In order to develop a simple detection assay for field use, the *T. Solium* T24 diagnostic protein was cloned and sequenced.

Inventors: Kathy Hancock, Fatima Williams, Victor Tsang, MelindaYushak, Sowmya Pattabhi
CDC Reference Number: I-009-03
Publication Number: WO2005000886

Trichomonas Vaginalis

Efficacy of Dicationic Compounds Against *Trichomonas Vaginalis*



Trichomoniasis has traditionally been treated with 5-nitroimidazole compounds, primarily metronidazole. However, an increasing recognition of *T. vaginalis* isolates that are resistant to metronidazole, combined with a number of individuals who are allergic to this medicine, suggests the need for alternative compounds to treat this infection. The dicationic compounds could fill this need.

Inventors: William Secor, Andrea Crowell, Chad Stephens, David Boykin, Arvind Kumar
CDC Reference Number: I-012-04
Publication Number: WO2005086754

RICKETTSIAL

Ehrlichia

Growing Ehrlichia Species in a Continuous Cell Line
Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. In the United States, ehrlichiosis is caused primarily by *E. chaffeensis*. The development of diagnostics and vaccines for these diseases has been hampered by a lack of continuous cell lines to produce large quantities of *Ehrlichia* antigens. In this invention, a method of growing pathogenic *Ehrlichia* species in the continuous monocyte-macrophage cell line DH82 has been developed.

Inventors: Jacqueline Dawson, Yasuko Rikihisa
CDC Reference Number: E-026-90

Patent Number: 5,192,679

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis
Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention includes the new species and an *Ehrlichia chaffeensis* infected cell line deposited with the American Type Culture Collection (ATCC) under accession number CRL 10679.

Inventors: Burt Anderson, Jacqueline Dawson
CDC Reference Number: E-029-91
Patent Number: 5,413,931

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis
Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention includes a PCR based diagnostic kit and methods for diagnosing ehrlichiosis in humans and for screening drugs.

Inventors: Burt Anderson, Jacqueline Dawson
CDC Reference Number: E-029-91
Patent Number: 5,789,176

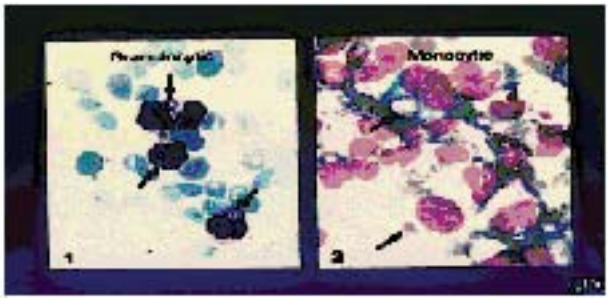
Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis
Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention relates to a composition comprising an immunogenic amount of *E. chaffeensis* antigen, either naturally produced or recombinant made, to induce antibodies against *E. chaffeensis*.

Inventors: Jacqueline Dawson, Burt Anderson
CDC Reference Number: E-029-91
Patent Number: 6,541,199

Identification of a New *Ehrlichia* Species from a Patient Suffering from Ehrlichiosis
Ehrlichiosis is non-communicable, rarely fatal, rickettsial disease found in the United States. It is clinically similar to Rocky Mountain Spotted Fever but lacks the distinctive rash and is related to Sennetsu Fever. A new isolate of the *Ehrlichia* species, *E. chaffeensis*, has been obtained from a patient suffering from ehrlichiosis. This invention relates to a composition comprising an immunogenic amount of *E. chaffeensis* antigen, either naturally produced or recombinant made, for use in an immunoassay and diagnostic kit.

Inventors: Jacqueline Dawson, Burt Anderson
CDC Reference Number: E-029-91
Patent Number: 6,524,590

Use of Human Immortalized Endothelial Cells to Isolate and Propagate *Ehrlichia chaffeensis* and *Ehrlichia canis*
Ehrlichiosis is non-communicable, rarely fatal disease found in the United States characterized by a sudden onset of fever, chills, malaise and sleeplessness which is related to Sennetsu Fever. Ehrlichiosis is clinically similar to *Rickettsia rickettsii*, Rocky Mountain Spotted Fever, but lacks the distinctive rash. This invention includes a purified immortalized human endothelial cell line infected with *Ehrlichia chaffeensis* or *Ehrlichia canis*.



Inventors: Jacqueline Dawson
CDC Reference Number: E-155-91
Patent Number: 5,401,656

Use of Human Immortalized Endothelial Cells to Isolate and Propagate *Ehrlichia chaffeensis* and *Ehrlichia canis*
Ehrlichiosis is non-communicable, rarely fatal disease found in the United States characterized by a sudden onset of fever, chills, malaise and sleeplessness which is related to Sennetsu Fever. Ehrlichiosis is clinically similar to *Rickettsia rickettsii*, Rocky Mountain Spotted Fever, but lacks the distinctive rash. This invention provides a method for simultaneously screening a human subject for *E. chaffeensis*, *E. canis*, or *Rickettsia rickettsii* by growing the organisms in human microvascular endothelial cells.

Inventors: Jacqueline Dawson
CDC Reference Number: E-155-91
Patent Number: 5,989,848

Novel Granulocytic *Ehrlichia* Genes and Uses Thereof
Granulocytic ehrlichiosis is an acute, potentially fatal tick-borne infection. This invention provides for granulocytic *Ehrlichia* specific genes encoding thirteen proteins that can be used as diagnostic reagents and vaccines. Isolated nucleic acid molecules, purified polypeptides, nucleic acid probes, and antibodies to the thirteen proteins are provided for. The recombinant nucleic acid molecule, vectors, cells and many other forms of the molecule are provided for along with the methods and kit for detection.

Inventors: Cheryl Murphy, Robert Massung
CDC Reference Number: I-011-99
Publication Number: WO0006744

SOFTWARE

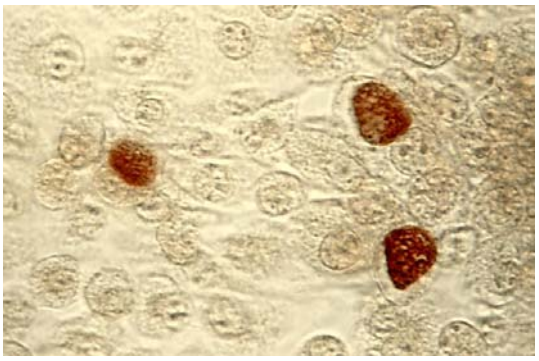
Disease Prevention

Family Healthware - Assessment, Classification, and Intervention Guide
Although family medical history has proven to be an important risk factor for many chronic diseases, it is under-used in the practice of preventive medicine. Existing tools are usually paper-based, time-consuming for the patient, and difficult to interpret for the health care provider. Family Healthware™ is a pc-based familial risk assessment tool. It is a three-step process which uses the disease history of a person's first-and second-degree relatives to assess the risk of common diseases of adulthood and influence early detection and prevention strategies. The risk assessment algorithms that support the tool provide results automatically and take minimal time and effort on the part of the health care provider. A resource manual provides the clinician with updated evidence-based guidelines for disease prevention and screening that are specific to a familial risk.

Inventors: Paula Woon, Maren Scheuner, Muin Khoury, Cynthia Jorgensen
CDC Reference Number: I-004-04

SEXUALLY TRANSMITTED DISEASES

Chlamydia



Methods and Compositions for the Simultaneous Detection of Multiple Analytes
Epidemiological and vaccine studies of *Streptococcus pneumoniae* and *Chlamydia* require serotype identification. Current methods of serotyping are labor intensive and subjective. This invention utilizes serotype specific antibodies bound to fluorescent beads which allows for simultaneous single tube capture and detection of all *S. pneumoniae* serotypes and three *Chlamydia* serotypes.

Inventors: Melinda Bronsdon, George Carlone, Joseph Martinez
CDC Reference Number: I-009-99
Publication Number: WO9945121

Syphilis

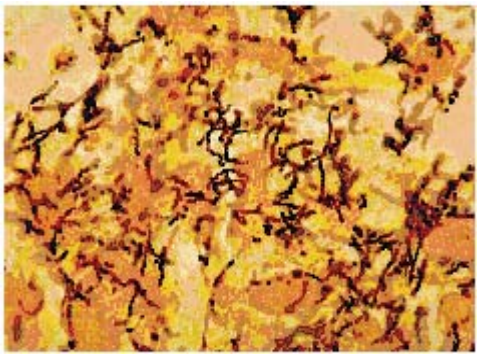
Attachment of Cardiolipin to Protein for Development of Non-Treponemal Antibody Assays
This invention comprises a method for reliably attaching cardiolipin to a solid substrate while maintaining its antigenicity, thus being useful for immunoassays for non-treponemal, or anti-lipoidal, antibodies. Currently there are no rapid, on-site

immunoassays for non-treponemal antibodies, such as those produced during an immune response from syphilis, partly because the antigens of the non-treponemal antibodies, e.g., cardiolipin, resist attachment to solid supports. Currently available tests require offsite lab work and are expensive to administer. This method overcomes the problems encountered in attaching cardiolipin and other antigens to a solid substrate and would allow the development of a class of strip-based tests (such as nitrocellulose strips) for non-treponemal, or anti-lipoidal, antibodies. This will allow inexpensive and rapid diagnosis of syphilis and most other tissue-damaging diseases.

Inventors: Arnold Castro, Huiying Wang, Robert George, David Cox
CDC Reference Number: I-007-06

DNA Polymerase from *Treponema pallidum**
Syphilis is caused by the spirochete *Treponema pallidum*. This invention provides the nucleic acid and amino acid sequences of the DNA polymerase I region of the *T. pallidum* genome and sequences of nucleic acid molecules that selectively hybridize with nucleic acid molecules encoding the DNA polymerase I enzyme from *T. pallidum* or certain complementary sequences that are described. The nucleic acid molecules are useful for the production of recombinant DNA polymerase I enzyme or as probes to detect the presence of *T. pallidum*. The nucleic acid and amino acid sequences are also useful as laboratory research tools to study the organism and the disease and to develop therapies and treatments for syphilis.

Inventor: Bret Steiner
CDC Reference Number: I-013-96
Patent Number: 6,020,128



Compositions and Methods for Detecting Syphilis Using Synthetic Antigens
Syphilis, a sexually transmitted disease, is caused by *Treponema pallidum*. If left untreated syphilis can cause destruction of the central nervous system and death. In the present invention, an antigen composition and sensitive and specific method for the detection of antibodies to *T. pallidum* are described. The composition is useful as an immunoreagent in immunoassays for the detection of antibodies associated with *T. pallidum* infection.

Inventors: Victoria Pope, William Morrill, Arnold Castro
CDC Reference Number: I-030-98
Patent Number: 6,815,173

Compositions and Methods for Detecting *Treponema pallidum*
Syphilis, a sexually transmitted disease, is caused by *Treponema pallidum*. If left untreated syphilis can cause destruction of the central nervous system and death. Methods for the specific and highly sensitive detection of *T. pallidum* infection comprising the use of specific antigenic proteins and peptides unique to *T. pallidum* are provided. In addition, the methods and compositions of the present invention are directed to the differential detection of specific *Treponema* infections enabling the identification of causative agents for specific *Treponema* disease states: syphilis (*T. pallidum* subspecies pallidum), yaws (*T. pallidum* subspecies pertenue), and bejel (*T. pallidum* subspecies endemicum).

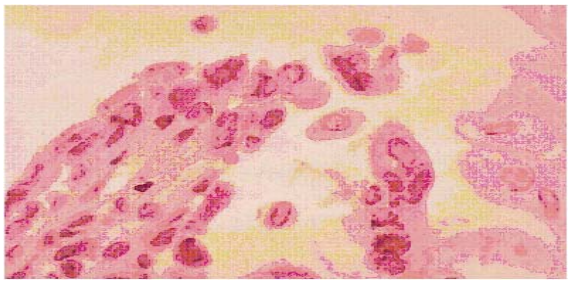
Inventors: Hsi Liu, Bret Steiner, Paul Maddon
CDC Reference Number: I-040-98
Publication Number: WO0077486

Immunological Immobilization of Cardiolipin Antigen to a Solid Support
A method for immobilizing a lipoidal antigen, comprising cardiolipin, lecithin, and cholesterol, on a solid support (such as a nitrocellulose membrane). The ability to immobilize a lipoidal antigen on a membrane satisfies a long felt need for membrane based assay for the detection of anti lipoidal antibodies.

Inventors: Arnold Castro, Robert George, Victoria Pope
CDC Reference Number: I-010-05

Herpes Virus

Novel Baculovirus Expression Vectors and Recombinant Antigens for Detecting Type-Specific Antibodies to Herpes Simplex Virus
The baculovirus expression vector system was used to express large amounts of herpes simplex virus (HSV) type-specific antigens. The ability to produce large amounts of antigen efficiently should help make accurate, simple, and reliable HSV type-specific serologic assays more widely available. This invention consists of a diagnostic assay for detecting type-specific HSV infection using recombinant baculovirus expressed HSV gG-1 and HSV gG-2 antigens.



Inventors: Demetrio Sanchez-Martinez, Philip Pellett
CDC Reference Number: E-021-91
Patent Number: 6,013,433

Novel Baculovirus Expression Vectors and Recombinant Antigens for Detecting Type-Specific Antibodies to Herpes Simplex Virus
The baculovirus expression vector system was used to express large amounts of herpes simplex virus (HSV) type-specific antigens. The ability to produce large amounts of antigen efficiently should help make accurate, simple, and reliable HSV type-specific serologic assays more widely available. This invention provides novel baculovirus transfer vectors constructed for efficient expression of foreign genes and novel baculoviruses expressing HSV glycoproteins IgG-1 and IgG-2.

Inventors: Philip Pellett, Demetrio Sanchez-Martinez
CDC Reference Number: E-021-91
Patent Number: 6,126,944

VETERINARY

Cat-Scratch Disease

Methods and Compositions for Diagnosing Cat-Scratch Disease and Bacillary Angiomatosis Caused by *Bartonella henselae*
Cat scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat-scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention provides a method of diagnosing cat-scratch disease and bacillary angiomatosis by detecting the presence of *B. henselae* or an immunogenically specific determinant thereof in humans or animals.

Inventors: Burt Anderson, Russell Regnery
CDC Reference Number: E-048-92
Patent Number: 5,399,485

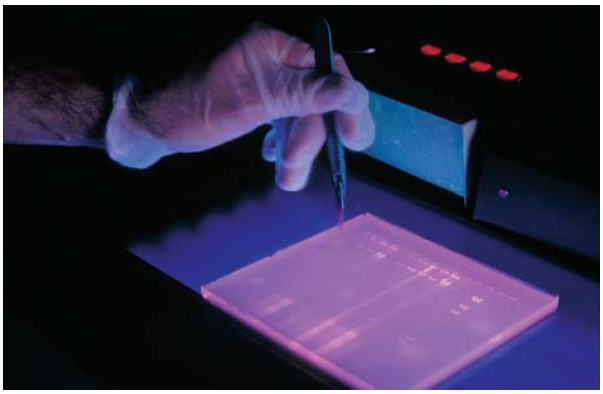
Compositions for Diagnosing *Bartonella henselae* and *Bartonella quintana* Infection
Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention allows for detection of small quantities of *B. henselae* and *B. quintana* in clinical samples and for differentiation between the two based on nucleic acid differences. The method of differentiation will be beneficial in the diagnosis of disease caused by the two organisms.

Inventors: Burt Anderson, Russell Regnery
CDC Reference Number: E-048-92
Patent Number: 5,644,047

Nucleic Acids Specific for *Bartonella quintana*
Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention provides a method of diagnosing *B. quintana* infection in a subject by detecting the presence of a nucleic acid specific to a purified heat shock protein of *B. quintana*.

Inventors: Russell Regnery, Burt Anderson
CDC Reference Number: E-048-92
Patent Number: 5,693,776

Nucleic Acids of *Bartonella henselae* and Methods and Compositions for Diagnosing *Bartonella henselae* and *Bartonella quintana* Infection
Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention identifies immunogenic peptides useful for identification of *B. henselae* and diagnosis of bacillary angiomatosis.



Inventors: Russell Regnery, Burt Anderson
CDC Reference Number: E-048-92
Patent Number: 5,736,347

Nucleic Acids of *Bartonella henselae* and Compositions for Diagnosing *Bartonella henselae* and *Bartonella quintana* Infection
Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention identifies immunogenic peptides useful for identification of *B. henselae* and diagnosis of bacillary angiomatosis.

Inventors: Burt Anderson, Russell Regnery
CDC Reference Number: E-048-92
Patent Number: 6,406,887

Composition to Protect a Mammal against *Bartonella henselae* Infection
Cat-scratch fever or bacillary angiomatosis is a bacterial disease transmitted via a cat scratch or bite. A previously unidentified, pathogenic species of *Bartonella* (formerly *Rochalimaea*), *B. henselae*, has been identified as the primary causative agent. A related species, *B. quintana*, may also produce illness in immunocompromised individuals. This invention relates to a therapeutic composition to protect a mammal from *B. henselae* infection that includes an isolated *B. henselae* antigen and adjuvant comprising a phosphazene polymer. Also included is a method to use such a therapeutic composition to protect a mammal from *B. henselae* infection. One embodiment is a method to protect a human from cat scratch disease by administering such a therapeutic composition to a domestic cat.

Inventors: Kevin Karem, Russell Regnery
CDC Reference Number: I-007-97
Patent Number: 5,958,414

Influenza

Genetic and Antigenic Structure of Canine Influenza Virus - Respiratory Disease in Dogs
The technology pertains to the isolated influenza virus that is capable of infecting canines and causing respiratory disease in the canine. The technology defines compositions and methods for inducing an immune response against an influenza virus of the present invention. The technology also details compositions and methods for identifying a virus of the invention and diagnosing infection of an animal with a virus of the invention.

Inventors: Ruben Donis, Jacqueline Katz, Alexander Klimov, Nancy Cox
CDC Reference Number: I-014-05

Rabies

Animal Vaccine for Simultaneous Sterilization And Rabies Control

This invention describes a vaccine that can be used on animals for simultaneous sterilization and rabies control. Stray animals are the main reservoirs for rabies on many countries. The two best non-lethal methods to control the spread of rabies in these populations are rabies vaccinations and sterilization. By incorporating the main receptor of sperm for fertilization into the rabies ERA virus, this invention would combine the two best methods to combat the spread of rabies in one vaccine. The vaccine can be quickly and inexpensively administered and can be used on many animals including dogs, cats, raccoons, and other wild animals that spread rabies.

Inventors: Xianfu Wu, Charles Rupprecht
CDC Reference Number: I-025-06

Vector for Recombinant Poxvirus Expressing Rabies Virus Glycoprotein

Rabies vaccines presently in use generally contain preparations of inactivated or attenuated live rabies virus. Such preparations might be relatively costly, biologically unstable, or produce vaccinal side effects. Hence, the need remains to provide for humans and animals an efficacious vaccine against rabies that would be potent, less perishable, less costly, and having diminished or no vaccinal side effects compared to present rabies vaccines. A vaccinia virus recombinant construct has been developed that expresses the gene for rabies virus glycoprotein. Recombinants may used for vaccines and could also be readily adapted for production of related antigen, antibody, and other immunobiological reagents

Inventors: Joseph Esposito, Kathleen Brechling, Bernard Moss
CDC Reference Number: E-359-86
Patent Number: 5,348,741

Raccoon Poxvirus as Gene Expression and Vaccine Vector for Genes of Rabies Virus and Other Organisms

In the United States, the wildlife species most involved in rabies transmission are skunks, raccoons, foxes, and insectivorous bats. Raccoons currently rank second to skunks as the major reservoir. Rabid foxes are a major source of the disease in Canada and many European countries. Although live-attenuated rabies virus vaccines are effective in immunizing foxes against rabies, they are not effective for immunizing skunks and raccoons. An oral rabies recombinant vaccine, based on a putative indigenous raccoon poxvirus, has been developed using raccoon poxvirus as the expression vector. The vaccine confers protection against rabies to a number of wild and domestic animals.

Inventors: Joseph Esposito, George Baer
CDC Reference Number: E-518-87
Patent Number: 5,266,313

Method of Sequencing Rabies Whole Genome and its Application in Vaccine Development

The critical feature of this technology is the ERA rabies whole genome DNA sequence. With the availability of the entire rabies genome, a recombinant vaccine can be developed using reverse genetics. The vaccines that can be developed using this genome are fundamentally different from classic ones that are being produced. The technology is being applied to other negative stranded RNA viruses.

Inventors: Xianfu Wu, Charles Rupprecht
CDC Reference Number: I-027-04

VIRAL

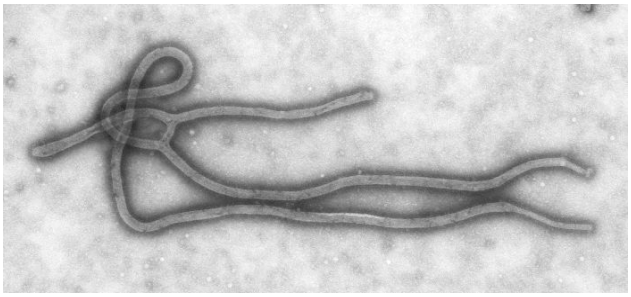
Astrovirus

Nucleic Acids Encoding Human Astrovirus Serotype 2 and Uses Thereof
Astroviruses are a cause of acute gastroenteritis in children and adults worldwide. The present invention provides a nucleic acid encoding human astrovirus serotype 2, or a unique fragment thereof. The sequence, a genomic RNA of human astrovirus serotype 2, contains 6,797 nucleotides, and is organized into three open reading frames. Also provided are purified antigenic polypeptide fragments encoded by the nucleic acid encoding human astrovirus serotype 2, or unique portions thereof. The sequence information of the present invention can be used to detect astroviruses in clinical specimens by utilizing PCR techniques. Additionally, the sequence data can be used to generate recombinant microorganisms expressing astrovirus capsid proteins and, subsequently, can be used to produce antigens for diagnosis of astrovirus infection.

Inventors: Roger Glass, Baoming Jiang, Stephen Monroe, Marion Koopmans
CDC Reference Number: E-059-93
Patent Number: 5,625,049

Ebola

Recombinant Infectious Molecular Clone of a Simian Foamy Virus (SFV) Expressing a Truncated form of the Ebola Virus Glycoprotein Gene
This invention involves the engineering of recombinant Simian Foamy Virus SFV (pFOV-7) which may be used to produce a vaccine for the Ebola virus infection. The engineered SFV elicits a protective immune response in the host by expressing a truncated Ebola virus gp gene (EbGP) as a fusion protein with SFV. This vaccine can be used by those at risk in endemic areas and by health professionals investigating outbreaks and treating patients. It may also as a vaccine to be used in the event an Ebola virus is used as a biological weapon.



Inventors: Thomas Folks, Anthony Sanchez, James Smith
CDC Reference Number: I-003-06

Enterovirus

Detection and Identification of Nonpolio Enteroviruses
Enteroviruses are one of the most common viruses infecting humans, causing illnesses ranging from mild (e.g., hand-foot-and-mouth disease and acute hemorrhagic conjunctivitis) to more serious disease (e.g., meningitis, paralysis, and encephalitis). Currently, no molecular reagents can distinguish between the 60+ enterovirus serotypes. CDC scientists developed this method to produce PCR primers capable of differentiating the 60+ serotypes of nonpolio enteroviruses (NPEVs).

Inventors: David Kilpatrick
CDC Reference Number: I-001-96
Patent Number: 6,618,917

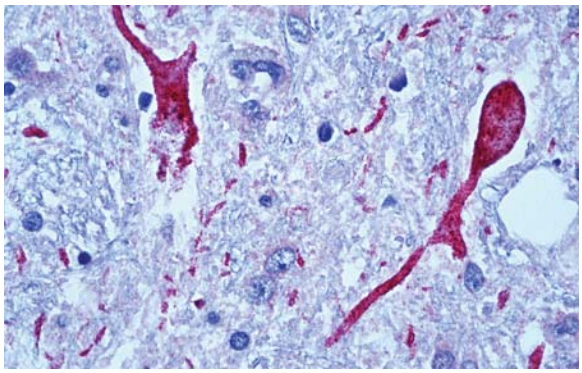
Typing of Human Nonpolio Enteroviruses
Enteroviruses infect 30-50 million Americans each year, resulting in 30-50,000 hospitalization for aseptic meningitis, as well as cases of acute flaccid paralysis, encephalitis, neonatal sepsis-like disease, and other illnesses. This invention provides a method for the rapid serotype identification of human enteroviruses, reducing the time required for typing from weeks to a few days. Application of the method will also provide data that may be useful for the development of additional virus-specific diagnostic reagents.

Inventors: Mark Pallansch, Kaija Maher, Steven Oberste, David Kilpatrick
CDC Reference Number: I-028-98
Patent Number: 6,846,621

Sensitive, Semi-nested PCR-Amplification of VPI Sequences for Direct Identification of Enteroviruses Serotypes from Orical Specimens
A reverse transcription/semi-nested polymerase chain reaction (RT-snPCR) assay was developed for detection and identification of enterovirus (EV) RNA in clinical specimens. The primers were designed for broad specificity and amplified all recognized and proposed EV serotypes and other antigenic variant strains tested. PCR products were successfully amplified and sequenced from cerebrospinal fluid, nasopharyngeal swabs, eye swabs, rectal swabs, and stool suspensions, allowing unambiguous identification of the infecting virus in all cases. The VP1 sequences derived from RT-scPCR products allow rapid phylonos.

Inventors: William Nix, Steven Oberste
CDC Reference Number: I-016-05

Flavivirus



Nucleic Acid Vaccines for Prevention of Flavivirus Infection
Mosquito borne viral encephalitis is often caused by a flavivirus such as Japanese encephalitis virus (JEV) or West Nile virus (WNV). This novel vaccine for flaviviruses comprises recombinant nucleic acids that contain genes for structural proteins of flaviviruses, such as JEV. These vaccines serve as a transcriptional unit for the biosynthesis of the virus protein antigens when administered in vivo. Furthermore, the invention provides for a method of immunizing a subject against infection by a flavivirus.

Inventor: Gwong-Jen Chang
CDC Reference Number: I-008-97
Publication Number: WO9963095

Nucleic Acid Vaccines for Prevention of Flavivirus Infection
The present invention encompasses isolated nucleic acids containing transcriptional units which encode a signal sequence of one flavivirus and an immunogenic flavivirus antigen of a second flavivirus or of a chimeric immunogenic flavivirus antigen comprising sequence from more than one flavivirus. The invention further encompasses a nucleic acid and protein vaccine and the use of the vaccine to immunize a subject against flavivirus infection. The invention also provides antigens encoded by nucleic acids of the invention, antibodies elicited in response to the antigens and use of the antigens and/or antibodies in detecting flavivirus or diagnosing flavivirus infection.

Inventors: Gwong-Jen Chang
CDC Reference Number: I-001-01
Publication Number: WO02081754

Hantavirus

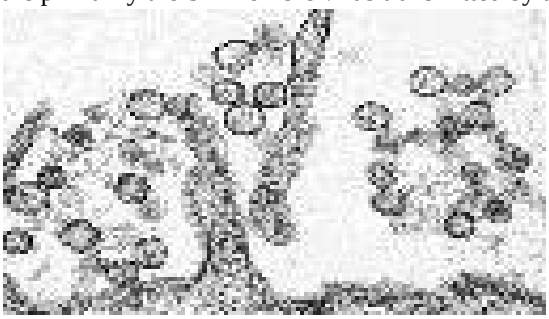
Nucleic Acid of a Novel Hantavirus and Reagents for Detection and Prevention of Infection
An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. The Sin Nombre strain identified in this invention (previously termed Four Corners virus) is the etiologic agent responsible for the outbreak of the adult respiratory distress syndrome (ARDS) in the Four Corners region of the United States. Hantavirus strains found in the southwestern U.S. are now known to be primarily the Sin Nombre strain of the virus.

Inventors: Thomas Ksiazek, Stuart Nichol, Christina Spiropoulou, Pierre Rollin
CDC Reference Number: E-183-93
Patent Number: 6,620,913

Nucleic Acids of a Novel Hantavirus and Reagents for Detection and Prevention of Infection
An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. The Sin Nombre strain (previously termed Four Corners virus) is the etiologic agent responsible for the outbreak of the adult respiratory distress syndrome (ARDS) in the Four Corners region of the United States. This invention includes nucleic acids of this newly discovered virus and nucleic acid reagents for use in methods of detection and prevention of infection by the virus.

Inventors: Stuart Nichol, Pierre Rollin, Christina Spiropoulou, Thomas Ksiazek
CDC Reference Number: E-183-93
Patent Number: 5,945,277

Black Creek Canal Hantavirus and Related Methods
An outbreak of acute respiratory distress syndrome in the spring of 1993 marked the emergence of rodent transmitted hantavirus infections as a recurring problem in the United States and Canada. Hantavirus strains found in the southwestern U.S. are primarily the Sin Nombre virus transmitted by the deer mouse. A previously unreported species of hantavirus is the causative agent of an outbreak in Florida. The virus responsible for this occurrence was isolated from cotton rats and represents a new and distinct serotype of hantavirus and is designated the Black Creek Canal hantavirus. This invention includes nucleic acids and antibodies for use in methods of detection and prevention of infection by the new virus.



Inventors: Sergey Morzunov, Thomas Ksiazek, Stuart Nichol, Pierre Rollin, Eugeny Ravkov
CDC Reference Number: E-183-93
Patent Number: 5,853,980

Bayou Hantavirus and Related Methods
The present invention relates to the discovery and isolation of a novel hantavirus designated the Bayou hantavirus. In particular, the present invention relates to nucleic acids of the newly discovered virus and to nucleic acid reagents (primers and probes), purified polypeptides and antibodies for use in methods of detection and prevention of infection by the virus. A vaccine or purified immunogenic polypeptide of the Bayou hantavirus in a pharmaceutically acceptable carrier is provided. A vector comprising the nucleic acids of the invention is provided. A method of detecting the presence of a hantavirus in a subject comprising contacting an antibody-containing sample from the subject with a purified polypeptide of the invention and detecting the reaction of the polypeptide and the antibody is provided. A method of detecting the presence of the Bayou hantavirus is provided comprising reverse transcribing viral RNA to synthesize a complementary DNA sequence followed by amplifying the DNA using primers which are selective for the Bayou hantavirus and detecting the presence of amplification, thereby indicating presence of the Bayou hantavirus in the sample.

Inventors: Pierre Rollin, Sergey Morzunov, Stuart Nichol, Thomas Ksiazek, Christina Spiropoulou
CDC Reference Number: E-183-93
Patent Number: 5,916,754

Hepatitis

Antigenically Reactive Regions of the Hepatitis A Virus Polyprotein
Hepatitis A (HAV) causes a transient illness, easily spread through contaminated water and food. While HAV infection is vaccine preventable, administration of the vaccine is usually restricted to epidemics and persons at increased risk. Vaccination in endemic countries may be inadequate. This invention provides for isolated, immunogenic HAV peptides corresponding to immunogenic epitopes of HAV. Moreover, various specific diagnostic embodiments utilizing these new discoveries are also disclosed.

Inventors: Howard Fields, Yuri Khudyakov
CDC Reference Number: I-005-96
Patent Number: 6,838,237

Neutralizing Immunogenic Hepatitis E Virus Polypeptides
Hepatitis E virus (HEV) is a recently discovered agent of enterically transmitted non-A, non-B hepatitis (ET-NANB). The disease remains a serious problem in many developing countries. Unlike other agents of viral hepatitis, HEV infection is often associated with high mortality rates in infected pregnant women. This recombinant protein is being utilized as a diagnostic reagent in the development of immunoassays for the detection of anti-HEV activity in human sera. This protein may also have potential for use as a vaccine to prevent HEV infection.

Inventors: Howard Fields, Yury Khudyakov, Jihong Meng
CDC Reference Number: I-013-00
Patent Number: WO0177156

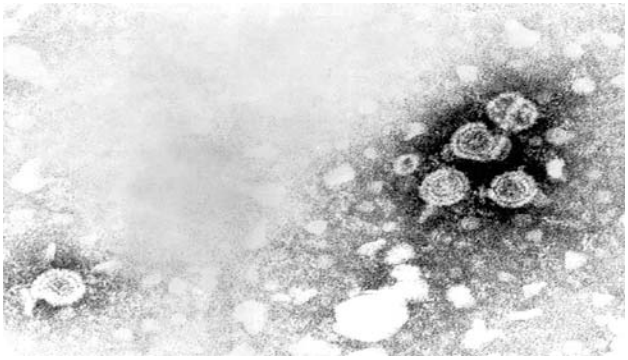
Synthetic Peptides Immunoreactive with Hepatitis A Virus Antibodies
Hepatitis A (HAV) virus causes a transient illness, easily spread through contaminated water and food. While HAV infection is vaccine preventable, administration of the vaccine is usually restricted to epidemics and persons at increased risk. Vaccination in endemic countries may be inadequate. In this invention synthetic peptides immunoreactive with HAV antibodies have been developed. The peptides are useful as laboratory reagents to detect or quantify HAV antibodies in biological samples, in clinical or research-based assays and for inducing an immune response to HAV when administered to a human or animal. The peptides contain antigenic epitopes, modified antigenic epitopes or combinations of epitopes of the major structural capsid polypeptides or non-structural polypeptides of HAV and contain one or more molecules of the amino acid glutamine at the carboxyl end of the peptide, which enhances immunoreactivity and immunogenicity, particularly IgM antibody reactivity.

Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: I-015-98
Publication Number: WO0105824

Mosaic Protein and Restriction Endonuclease Assisted Ligation Method for Making the Same
This invention consists of a mosaic protein comprising a variety of immunoreactive antigenic epitopes from several genotypes of hepatitis C virus. The mosaic protein provides a sensitive and specific immunological hepatitis detection assay. A restriction enzyme assisted ligation method of making an artificial gene permits controlled construction of mosaic proteins, and allows confirmatory expression of the intermediate gene products.

Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: I-018-97
Patent Number: 6,030,771

Mosaic Protein and Restriction Endonuclease Assisted Ligation Method for Making the Same
This invention consists of mosaic nucleic acids encoding a variety of immunoreactive antigenic epitopes from several genotypes of hepatitis C virus. The mosaic nucleic acid provides a sensitive and specific immunological hepatitis detection assay. A restriction enzyme assisted ligation method of making an artificial gene permits controlled construction of mosaic proteins, and allows confirmatory expression of the intermediate gene products.



Inventors: Yuri Khudyakov, Howard Fields
CDC Reference Number: I-018-97
Publication Number: WO9910506

Antigenic Epitopes and Mosaic Polypeptides of Hepatitis C Virus Protein
Hepatitis C (HCV) virus has emerged as a significant public health problem due to widespread infection from blood transfusions given prior to the availability of routine screening. It also continues to be a significant problem in countries with substandard health care practices. This invention comprises a single artificial gene composed of immunodominant epitopes. The expressed protein has significant diagnostic relevance for the detection of antibodies to HCV. Accordingly, this invention is useful as reagents for the diagnosis or monitoring of HCV in a biological sample. These epitopes and polypeptides are also useful for the construction of immunogenic pharmaceutical compositions such as vaccines.

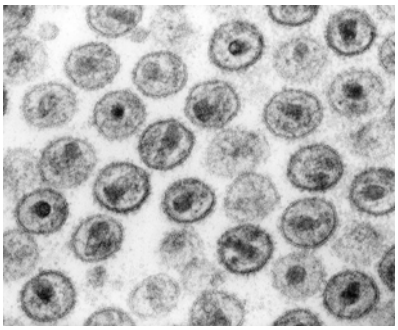
Inventors: Howard A Fields, Yuri Khudyakov
CDC Reference Number: I-022-98
Publication Number: WO0104149

HIV

A Simple Assay for Detecting Recent HIV-1 Infection and Estimating Incidence
Inventors: Steve McDougal, Bharat Parekh
CDC Reference Number: I-021-02

Development of a Chimeric Recombinant HIV-1 Envelope Protein Derived from Immunodominant Region (IDR) of Multiple Subtypes
A recombinant HIV protein (rIDR-M) in *E. coli*. The recombinant protein incorporates 3 sequences derived from immunodominant region of gp41, representing divergent HIV-1 subtypes A through E (group M). The protein has a Histidine tag at the N-terminus which helps in purification of the protein. In addition, 3 sequences are separated by hydrophilic spacer sequences to increase yield and solubility of the purified recombinant protein. It has been shown to detect HIV antibodies to divergent HIV-1 viruses with high sensitivity. This technology also details a process that has been developed to produce significant quantities of purified rIDR-M from E. Coli, providing a continuous source of consistent product.

Inventors: Bharat Parekh, Xierong Wei, Steve McDougal
CDC Reference Number: I-002-04



Method and Kit for Detecting Resistance to Antiviral Drugs
One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention provides for an assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drug in a biological sample.

Inventors: Shinji Yamamoto, Gerardo Lerma, William Switzer, Walid Heneine, Thomas Folks
CDC Reference Number: I-005-98
Patent Number: 6,787,126

Method and Kit for Detecting Resistance to Antiviral Drugs
One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention adds multi-drug resistance testing to the assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drugs described in I-005-98.

Inventors: Walid Heneine, Shinji Yamamoto, Gerardo Lerma, William Switzer, Thomas Folks
CDC Reference Number: I-004-02
Publication Number: 20050170339

Methods and Compositions for Inhibition of Viral Replication
This invention relates to the identification of a cellular enzyme (casein kinase II) which, when inactivated by chemical inhibitors, results in the inability of the cell to support the replication of HIV-1. This discovery is unique because the drug target is cellular rather than viral, which may greatly reduce the ability of the virus to develop resistance to the drug. Since there are no anti-HIV-1 drugs currently available which have this property, the present invention fills the need to develop novel HIV-inhibitory agents for possible therapeutic use.

Inventors: Jennifer Brown, Thomas Folks, Walid Heneine, Paul Sandstrom, William Switzer
CDC Reference Number: I-012-96
Patent Number: 6,274,611

Methods and Reagents for Molecular Detection of HIV-1 Groups
This invention provides reagents and assays for detecting HIV-1 groups M and O and optionally HIV-1 group N and SIVcpz. Nucleic acid primers for the hybridization to, amplification, and subsequent detection are also provided for. The nucleic acid amplification assays can detect small concentrations of HIV and are also useful for qualitative and quantitative examinations.

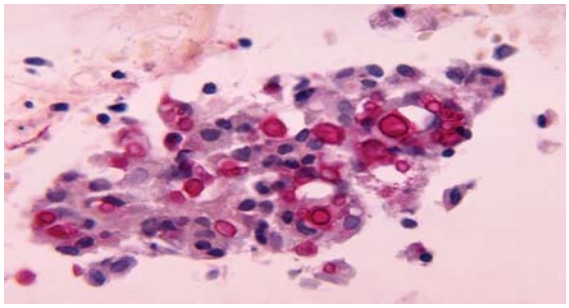
Inventors: Danuta Pieniazek, Chunfu Yang, Renu Lal
CDC Reference Number: I-020-98
Publication Number: WO0046403

Cytotoxic T Cell (CTL) Epitopes of HIV (Subtype E): Reagents for Research, Drug Studies and HIV Vaccines
Identification of promiscuous or multi-determinant T cell epitopes is essential for HIV vaccine development; however, current methods for T cell epitope identification are both cost intensive and labor intensive. We have developed a computer-driven algorithm, named EpiMer, which searches protein amino acid sequences for putative MHC class I-restricted T cell epitopes. Since EpiMer-predicted peptides have the potential to bind to multiple MHC alleles, they are strong candidates for inclusion in a synthetic HIV vaccine.

Inventor: Janet McNicholl
CDC Reference Number: I-033-98
Publication Number: WO02069691

Development of a HIV-1 Multi-Clade, Multivalent (HIV1MCMV) Recombinant Vaccine Construct

Most HIV-1 vaccine constructs are subtype-specific and designed to prime only one arm of the immune system. Thus, they are not expected to protect against diverse natural HIV-1 infections. Data from vaccine trials suggest that additional epitopes as well as activation of both arms of the immune system may be required for an effective HIV-1 vaccine. As the HIV epidemic continues to spread world wide, the need for an effective vaccine remains urgent. This invention addresses this need through a multi-epitope, multi-clade HIV1 vaccine construct that will provide a universal vaccine for all parts of the world affected by the epidemic. The design of the construct allows for the addition or deletion of epitopes and contains specific cellular targeting epitopes that should permit optimization for better antigen processing and recognition. The construct might be combined with other epitope based constructs to develop multi-pathogen vaccines.



Inventors: Renu Lal, Sherry Owen
CDC Reference Number: I-013-03
Publication Number: WO2004085466

DNA Expression Vectors and Methods of Use

This invention provides novel plasmid constructs useful as vectors for the delivery of DNA vaccines. The novel plasmid constructs can include vaccine inserts derived from pathogenic viruses, bacteria, parasites, or fungi. In particular, non-infectious DNA vaccines for the reduction of the human immunodeficiency virus (HIV) burden of infected persons are offered. These provide effective means to treat and/or prevent and HIV/AIDS related infection.

Inventors: Dennis Ellenberger, Harriet Robinson, Ted Ross, Rick Bright, Jian Hua, James Smith, Bernard Moss, Thomas Folks, Salvatore Butera, Rama Amara, Linda Wyatt, Patricia Earl, Donald Hildebrand, Janet McNicholl
CDC Reference Number: I-015-01
Publication Number: WO03076591

Development of a Rapid HIV Diagnostic Assay for Diagnosis and Detection of Recent and Long Term HIV-1 Infection

This technology provides the necessary information for the development of a device for simultaneous rapid diagnosis of HIV infection and for identification of recent HIV-1 infection. The device will utilize immunochromatographic or flow-through principles to detect HIV antibodies. The device will have two areas, one for diagnosis of HIV infection and a second to distinguish recent infection (<6 months) from long-term infection. The addition of this second area can have added significance for surveillance, counseling, partner notification and other prevention activities, including the estimation of HIV incidence in cross-sectional populations. The proposed device would utilize a single platform that contains all of the required reagents, making it simple and easy to use. The entire testing process, including the determination of incident infections, will be done in less than 20 minutes. The detection of recent infection is important for incidence measurements and for targeting prevention activities and resources. Incidence also serves as an indicator of the effectiveness of intervention strategies. The demand for incidence is increasing worldwide as the global effort to reduce the spread of AIDS expands.

Inventors: Timothy Granade, Bharat Parekh, Chou-Pong Pau
CDC Reference Number: I-003-04

Development and Characterization of Large Volume Panels of Plasma, PMBC, and DBS from HIV Strains from West Africa

There is expanding interest in using new and existing diagnostic and clinical assays for detecting and monitoring HIV infections in Africa. Currently, large volume panels of serologically and genetically characterized HIV-1 subtypes and recombinant strains from West and Central Africa do not exist for evaluating the type of diversity found in these regions. CDC has obtained a large number of discarded blood bank samples from these regions. Characterization of these samples provide a unique and valuable set of reagents for vaccine trials, quality assurance, quality control, proficiency panels, and evaluation of new and existing serologic and genetic assays for use in Africa. Select samples have viable cell cultures and whole genome sequences available.

Inventors: Marcia Kalish, Salvatore Butera, Thomas Folks, Danuta Pieniazek, Amanda Schaefer, Ae Saekhou Youngpairoj, John Nkengasong
CDC Reference Number: I-006-04

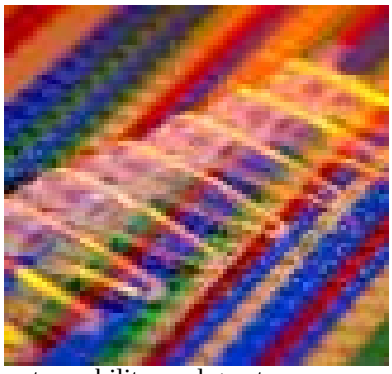
Multiple Antigenic Peptide Assay for Detection of HIV or SIV Type Retroviruses
Human immunodeficiency virus (HIV) is subdivided into 2 types, HIV-1 and HIV-2, both of which are believed to be the result of zoonotic transmission. Humans are being increasingly exposed to many different simian immunodeficiency viruses (SIVs) in wild primates, for example through the hunting and butchering trade in Africa. This human exposure to SIVs may lead, or has already led, to transmission of SIVs with the potential to cause new epidemics. Unfortunately, new zoonotic transmissions may go undetected because of the lack of SIV-specific tests. Thus, there is the potential to compromise the safety of the blood donor supply system and possibly to seed a new HIV-like epidemic. This invention addresses these problems by providing a way to test for the many divergent strains in monkeys and humans to identify primary infection and prevent secondary transmission.

Inventors: Marcia Kalish, Tom Folks, William Switzer, Chou-Pong Pau, Clement Ngondmo
CDC Reference Number: I-023-02

RAB9 and Uses Thereof Related to Infectious Disease
Methods of reducing the activity of Rab9A or Rab11A, by reducing the activity of a modulator thereof that increases Rab9A or Rab11A activity, to treat or reduce infection or other stage of the life cycle of a pathogen, such as a virus. The technology also addresses methods of identifying agents involved in pathogen infection, such as modulators of Rab9A and Rab11A.

Inventors: Thomas Hodge, Natalie McDonald, Donald Rubin, Michael Shaw, Anthony Sanchez, James Murray
CDC Reference Number: I-036-04
Publication Number: WO2005092924

Simple, Rapid, and Sensitive Real-Time PCR Methods for Detecting Drug Resistance in Human Immunodeficiency Viruses (HIV)



Mutations that confer resistance to antiretroviral drugs are expected to increase as use of these drugs for the clinical management of HIV-1 infected people increases worldwide. Resistance-related mutations are conventionally detected by sequence analysis of viral RNA from plasma. The sensitivity limitations of conventional sequence analysis make it difficult to measure low levels of mutants, such as what might be present early in the emergence of resistance or which might persist at low set points in the absence of treatment. Real-time PCR assays can provide a more user-friendly, less expensive, and more sensitive method for detecting drug resistance-associated mutations, and thus, can be a powerful screening tool for surveillance and as a cost effective screen for treatment-related resistance. This invention allows real-time PCR-based testing for different point mutations in patient samples at an achievable sensitivity of 1-2 log greater than conventional sequencing. The assay measures the differential amplifications of common and mutation-specific reactions that target codons of interest. Given the low cost, high-throughput capability, and greater sensitivity than conventional testing, these assays will be useful for detecting drug resistance-associated mutations and could aid in the clinical management of HIV-1 infection.

Inventors: Jeffrey Johnson, Walid Heneine
CDC Reference Number: I-005-03

Recombinant Infectious Clone of Simian Foamy Virus (SFV) Expressing HIV-1 gp 120 for Vaccine Purposes
This invention uses a reengineered Simian Foamy Virus (SFV) to deliver long term immunization against HIV to patients. An HIV-1 gene is inserted into an infectious molecular clone of SFV and injected into the patient, thus causing the host's own cells to produce the gp120 glycoprotein for the life of the infected cells. As a result, the recombinant SFV clone constantly stimulates immune system and sustains antibody response to HIV, thereby obviating the need for booster immunizations. SFV has distinct advantages over other delivery methods because it causes no harm to the host and is rarely seen in the human population.

Inventors: Thomas Folks, James Smith
CDC Reference Number: I-004-06

Prevention of Rectal SHIV Transmission
This invention discloses the use of a Tenofovir/FTC Combination to prevent rectal SHIV transmission. Available data shows that Tenofovir alone is not sufficient to protect against SHIV mucosal infection. This invention shows chemoprophylaxis in combination with retrovirals provides a high level of protection against not only initial viral exposure, but also repeated virus challenges.

Inventors: Walid Heneine, Thomas Folks, J. Gerardo Garcia-Lerma, Ronald Otten
CDC Reference Number: I-022-06

Human Papillomavirus

Human Papillomavirus (HPV) Variant Assignment by Pyrosequencing
Human Papillomavirus (HPV) has been associated with an increased risk of cervical disease. Currently available tests only detect HPV in samples containing one variant and use conventional and slow viral genome DNA sequencing. This invention uses pyrosequencing to allow for rapid sequencing and detection of multiple HPV variants.

Inventors: David Swan, Kara L. Duncan, Mangalathu S. Rajeevan, Elizabeth R. Unger, Josef Limor
CDC Reference Number: I-028-05

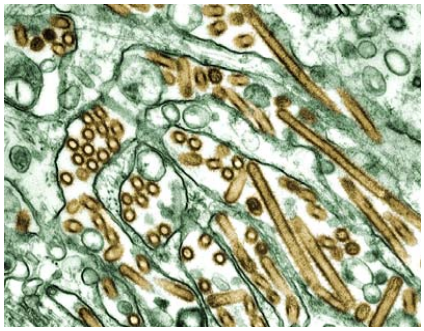
Influenza

High Growth Reassortant Avian Influenza Virus with an Avirulent Hemagglutinin
An engineered avian virus that has the necessary features for use in the production of a vaccine against strains of highly pathogenic avian influenza which are currently circulating in Asia

Inventors: Yumiko Matsuoka, Ruben Donis, Alexander Klimov
CDC Reference Number: I-012-05, I-018-05

Preparation and Use of Recombinant Influenza A Virus M2 Constructs and Vaccines
M2, a structurally conserved influenza A viral surface protein, is capable of inducing broader, more cross-reactive immunity to type A influenza viruses. This invention solves the problems of the prior art approaches to recombinant M2 production by providing new recombinant forms of M2 whose structure has been modified to allow simple prokaryotic expression as a soluble, readily purified variant protein which retains antigenic and immunogenic properties. The invention relates to vaccines comprised of these new recombinant forms of M2, and to methods of prevention and treatment of influenza A virus infections.

Inventors: Jacqueline Katz, Alan Frace, Alexander Klimov
CDC Reference Number: I-020-97
Patent Number: 6,169,175



Primer and Probes for Detection and Discrimination of Types and Subtypes of Influenza Viruses by Real-Time RT-PCR
This method allows for a rapid detection and identification of types and subtypes of influenza viruses. This includes avian influenza subtypes that have been shown to infect humans and may have pandemic potential. This protocol includes the only available primer/probe sets to specifically and sensitively detect highly pathogenic H5N1 viruses circulating currently in South East Asia.

Inventors: Stephen Lindstrom, Alexander Klimov, Nancy Cox, Lamorris Loftin
CDC Reference Number: I-007-05

Vaccine Against Pandemic Strains of Influenza Viruses
The genetic re-assortment between human and avian influenza viruses can result in a virus with a novel HA, typically of avian origin, against which humans lack immunity. In the 20th century, the pandemics of 1918, 1957, and 1968 were the result of such antigenic shifts. The recent outbreaks of avian influenza caused by H5N1 (ongoing in South East Asia), H7N7 and H9N2 viruses with infections of humans have created a new awareness of the pandemic potential of these viruses that circulate in domestic poultry. The currently available subtype-specific vaccines offer limited protection against heterologous strains. Thus, there is a need for new nonpathogenic replication-defective adenoviral vector-based vaccines that provide long-lasting and broad immunity against pandemic influenza strains. The present invention discloses immunogenic compositions with native or

modified HA gene(s) from avian influenza viruses of pandemic potential alone or in combination with NA and or other internal genes of H1N1 or H2N2 or H3N2 or avian viruses expressed with adenoviral vector.

Inventors: Suryaprakash Sambhara, Jacqueline Katz, Mary Hoelscher, Suresh Mittal, Dinesh Singh
CDC Reference Number: I-006-05

DNA Microarray Diagnostic for Emerging Strains of Influenza A
This invention describes a DNA microarray called "FluChip" that will quickly and simply identify infection of influenza virus and characterize the virus's type and antigenic sub-type. This chip could be used in the world-wide influenza surveillance network operated by the World Health Organization and could play a key role in the rapid response to influenza outbreaks.

Inventors: Catherine Smith, Nancy Cox, Kathy Rowlen, Robert Kuchta, Michael Townsend, James Smagala, Chad Moore, Erica Dawson, Martin Mehlmann
CDC Reference Number: I-021-06

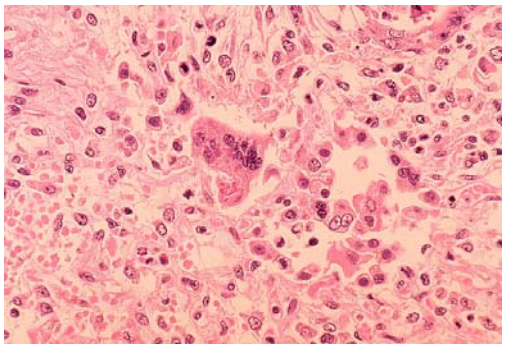
Lymphotropic

Novel Human T-Cell Lymphotropic Virus, Designated HTLV-3
The Human T-Cell Lymphotropic Virus (HTLV) is known to cause leukemia, lymphomas, and neurological diseases and is part of routine blood screening. The present invention discloses novel HTLV viruses which are distinct from HTLV1 and HTLV-2 and more related to simian T-cell lymphotrophic viruses, type 3 and 4. The viruses, tentatively called HTLV-3 and HTLV-4 may be endemic among humans and are likely the human counterparts to STLV-3 and STVL-4. Like HTLV-1 and HTLV-2, these viruses may be the causative agents of human diseases.

Inventors: William Switzer, Walid Heneine, Thomas Folks, Nathan Wolfe, Donald Burke, Eitel Mpoudi-Ngole
CDC Reference Number: I-019-04

Measles

Measles Virus Specific Antibody Detection Using Recombinant Measles Proteins
Current technology for measles virus detection relies on the use of whole virus and antigen in an enzyme immunoassay format. Generation of a recombinant nucleoprotein in the baculovirus expression vector system eliminates the use of whole virus and supplies an abundant source of antigen necessary for the evaluation of seroconversion and seroprevalence rates within vaccinated populations. Additionally, use of this recombinant antigen provides greater reproducibility with decreased cross-reactivity to human serum proteins.



Inventors: Kimberly Hummel, Dean Erdman, William Bellini, Janet Heath
CDC Reference Number: E-043-92
Publication Number: WO9322683

Poliovirus

Modulation of Poliovirus Replicative Fitness by Deoptimization of Synonymous Codons
Infections by intracellular pathogens such as viruses, bacteria and parasites, are cleared in most cases after activation of specific T cellular immune responses that recognize foreign antigens and eliminate infected cells. Vaccines against those infectious organisms have been traditionally developed by administration of whole live attenuated or inactivated microorganisms. Although research has been performed using subunit vaccines, the levels of cellular immunity induced are usually low and not capable of eliciting complete protection against diseases caused by intracellular microbes. However, CDC inventors discovered that replacement of one or more natural (or native) codons in a pathogen with synonymous unpreferred codons can decrease the replicative fitness of the pathogen, thereby attenuating the pathogen. The unpreferred synonymous codon(s) encode the same amino acid as the native codon(s), but have nonetheless been found to reduce a pathogen's replicative fitness. This invention teaches compositions and methods that can be used to develop attenuated vaccines having well-defined levels of replicative fitness and enhanced genetic stabilities.

Inventors: Olen Kew, Cara Burns, Jing Shaw, Raymond Campagnoli, Jacqueline Quay
CDC Reference Number: I-025-04

Orthopoxvirus

Monoclonal Antibodies Specific for Variola Virus

This technology comprises two series of monoclonal antibodies which specifically recognize the variola virus which causes smallpox. The first monoclonal recognizes variola but not other closely related orthopox viruses in ELISA assays, while the second monoclonal recognizes variola as well as camelpox and other related orthopox viruses. The antibodies can be used to create novel tests for variola virus using both clinical and environmental samples. They also may be used to study the biology of the variola virus during infection and create therapeutic treatments.

Inventors: Inger Damon, Scott Smith, Joanne Patton, Kevin Karem, Dennis Bagarozzi, John Hart, John Kools, Gin Lou
CDC Reference Number: I-009-06

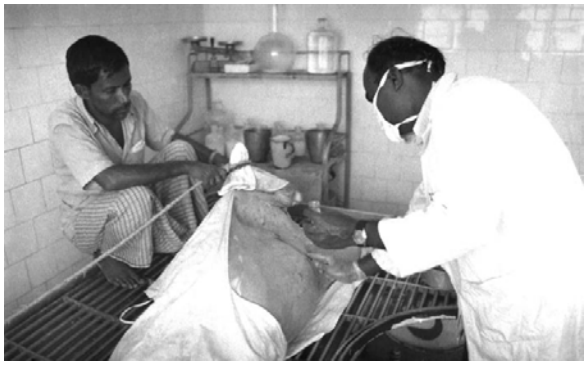
Diagnostic Assay for Orthopoxviruses Other than Variola

A new real-time PCR based diagnostic assay was designed that targets the DNA polymerase gene of all Eurasian orthopoxviruses other than variola (smallpox). This gene target is highly conserved and required for a productive viral life cycle, ensuring all infectious orthopoxviruses will retain this gene. The assay assists in the diagnosis of orthopoxviral infections (ex. vaccinia, cowpox, monkeypox) which affect humans. Since the assay does not detect variola, a rash illness can be confirmed as an orthopoxviral infection that is not smallpox at the same time. The assay is also much more sensitive than available standard PCR tests.

Inventors: Yu Li, Inger Damon, Victoria Olson
CDC Reference Number: I-026-04

Diagnostic Assay for Cowpox

This real-time PCR based assay accurately detects trace amounts of cowpox. Unlike currently available tests, this real-time PCR assay uniquely identifies cowpox among all possible orthopox viruses using a small region of DNA found uniquely in the cowpox species of orthopox viruses. This assay can successfully identify cowpox when the clinical sample contains as few as 150 viral copies. As a result, this test is much faster and more sensitive than currently available PCR tests.



Inventors: Yu Li, Inger Damon
CDC Reference Number: I-034-05

Therapeutic Treatment of Poxvirus Infections

This invention covers an antiviral-like therapeutic treatment for Poxvirus, the cause of Monkeypox, Molluscum Contagiosm, Smallpox, and other diseases. In *in vitro* experiments, this compound substantially reduced the amount of plaques formed. As a result, this drug may be developed for therapeutic treatment of Poxvirus infections. Such treatments could be especially important in the event of a smallpox outbreak, as vaccinations against the virus have not been widely administered for the last thirty years.

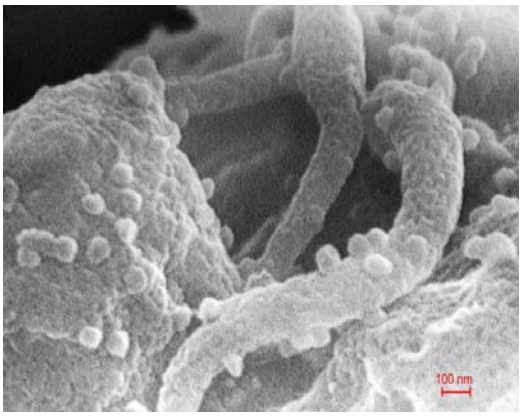
Inventors: Kemba Lee, Russell Regnery
CDC Reference Number: I-019-06

Retrovirus

Methods for Sensitive Detection of Reverse Transcriptase

Retroviruses are widely distributed in vertebrates and are known to cause a variety of diseases in man and animals including immunodeficiencies, leukemias and lymphomas. The entire retrovirus family is characterized by the presence of a unique enzyme, reverse transcriptase (RT), which transcribes the viral genomic RNA into a double-stranded DNA copy. This invention provides a method for detecting a retrovirus in a biological sample by identifying the presence of RT, and further allows for differentiating between infection by HIV-1 Group M and Group O in a HIV-1 infected subject.

Inventors: Thomas Folks, Walid Heneine, William Switzer, Shinji Yamamoto
CDC Reference Number: E-232-93
Patent Number: 5,849,494



Methods for Sensitive Detection of Reverse Transcriptase
Retroviruses are widely distributed in vertebrates and are known to cause a variety of diseases in man and animals including immunodeficiencies, leukemia's and lymphomas. The entire retrovirus family is characterized by the presence of a unique enzyme, reverse transcriptase (RT), which transcribes the viral genomic RNA into a double-stranded DNA copy. This invention provides a method for detecting a retrovirus in a biological sample by identifying the presence of RT.

Inventors: Shinji Yamamoto, Walid Heneine, William Switzer, Thomas Folks
CDC Reference Number: E-232-93
Patent Number: 6,136,534

Method and Kit for Detecting Resistance to Antiviral Drugs
One of the problems with the development of current therapies for HIV infection is that the HIV virus rapidly develops resistance to drugs such as reverse transcriptase inhibitors. This invention provides for an assay and kit for the detection of phenotypic resistance to a reverse transcriptase inhibitor drug in a biological sample.

Inventors: Shinji Yamamoto, Gerardo Lerma, William Switzer, Walid Heneine, Thomas Folks
CDC Reference Number: I-005-98
Publication Number: 6,787,126

Compositions, Methods and Devices for Detection of Retroviral Infection
Currently, there are shortages of organs, tissues and cells for transplantation into humans. These shortages, combined with recent advances in transplantation immunology, have provided impetus for the development of xenotransplantation - the therapeutic use of living animal tissues and organs in humans. Pigs are among the primary species proposed as sources of xenografts. In response to recent concerns regarding the transmission of infectious agents from animals to humans, a method was developed to detect porcine retroviral agents. This method detects the presence of human antibodies created in response to exposure to such agents in a xenotransplant recipient.

Inventors: Walid Heneine, William Switzer, Thomas Folks, Paul Sandstrom, Aprille Matthews
CDC Reference Number: I-021-98
Patent Number: 6,596,478

Methods and Devices for Detection of Xenogenic Graft Persistence
Currently, there are shortages of organs, tissues and cells for transplantation into humans. These shortages, combined with recent advances in transplantation immunology, have provided impetus for the development of xenotransplantation - the therapeutic use of living animal tissues and organs in humans. Pigs are among the primary species proposed as sources of xenografts. In response to recent concerns regarding the transmission of infectious agents from animals to humans, a method was developed to detect porcine endogenous retroviral (PERV) agents. The compositions, methods and devices are useful for determining or monitoring graft survival and rejection in recipients of xenografts and are useful for detecting PERV infections in a xenotransplant recipient or donor. In addition, the compositions, methods and devices are useful for screening therapeutic products to be administered to humans to ensure that the products are free of PERV contamination prior to administration.

Inventors: William Switzer, Shanmugam Vedapuri, Walid Heneine
CDC Reference Number: I-024-98
Patent Number: 6,566,102

Respiratory Syncytial Virus

Compositions and Methods for Modulating RSV Infection and Immunity
RSV is the single most important cause of lower respiratory tract disease in children. Many vaccination strategies have been attempted, but as of yet none have been successful. This invention relates to the discovery of functional motifs in the RSV G protein that may provide new insights into the past vaccine failures and may lead to immunogenic modifications that would provide a safe and efficient RSV vaccine.

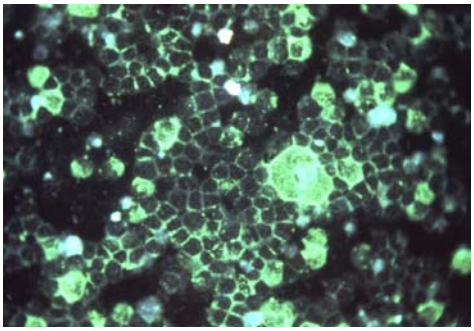
Inventors: Ralph A Tripp, Les Jones, Larry J Anderson
CDC Reference Number: I-022-00

Publication Number: 20040009177

CD40 Ligand Adjuvant for Respiratory Syncytial Virus
Respiratory syncytial virus (RSV) has long been recognized as a major viral pathogen of the lower respiratory tract of infants. Successful methods of treating or preventing RSV are currently unavailable. CD40 ligand (CD40L) is an important costimulatory molecule on the T-cell and is central to the development of immunity. CD40L can be used as an adjuvant to enhance cytokine and antibody response to RSV.

Inventors: Ralph Tripp, Michael Brown
CDC Reference Number: I-029-99
Publication Number: WO0156602

Macroaggregated Albumin-Polyethylenimine (MAA-PEI) Lung-Targeted Delivery of RSV DNA Vaccines
Currently, no safe and effective RSV vaccine is available. DNA vaccines encoding RSV F or G glycoproteins are one RSV vaccine option being examined for safety and efficacy. However, DNA vaccination has been problematic because of the need for repeated vaccination requiring large amounts of DNA, and DNA vaccination does not often result in mucosal immunity. Macroaggregated albumin (MAA) has been used for many years in imaging pulmonary blood flow, as the size of MAA results in these particles being trapped in the lung arterioles. This invention demonstrates that MAA conjugated to polyethylenimine (MP) is a useful carrier to deliver RSV-DNA vaccines to the site of RSV infection (lungs) and may be effective at enhancing RSV immunity.



Inventors: Ralph Tripp, Jennifer L. Harcourt
CDC Reference Number: I-026-01
Publication Number: 20040009903

Rotavirus

Rotavirus Strain G9P11
Viral gastroenteritis is an acute diarrheal disease which can cause severe dehydration and complications, especially in young children. Rotaviruses are the single most important etiologic agents of viral gastroenteritis of infants and young children world-wide and cause 35-50% of hospitalizations for this condition during the first 2 years of life. This invention includes a modified rotavirus of the strain G9P11, and an isolated nucleic acid encoding the rotavirus of strain G9P11 and a purified antigen specific for the rotavirus which may be used to provide protection against rotaviral infection.

Inventors: Roger Glass, Bimal Das, Jon Gentsch, Maharaj Bhan
CDC Reference Number: E-122-94
Patent Number: 5,773,009

Novel Method to Inactivate Rotavirus
This invention describes a new method for inactivating a rotavirus while preserving the virus's proteins and antigenicity. Previous methods to inactivate the virus used formalin and beta-propiolactone, which were found to alter the rotavirus proteins and reduce its antigenicity. As a result, vaccines based upon these inactivated viruses were either partially or completely ineffective. This method accomplishes the same result while maintaining the virus's antigenicity for vaccination purposes. The invention also describes a method for vaccinating children against rotavirus diarrhea in both developed and developing countries.

Inventors: Baoming Jiang, Roger Glass, Jean-Francois Saluzzo
CDC Reference Number: I-010-06

New Parenteral Human Rotavirus Vaccine Strains CDC-6, CDC-7, CDC-8, and CDC-9
This invention describes methods for adapting and producing human rotavirus vaccine strains to serve as an alternative to live oral rotavirus vaccinations and can prevent or control severe rotavirus diarrhea among children worldwide. These strains are produced in Vero cells, and the four new parenteral human rotavirus vaccine strains covered by this invention are representatives of common rotavirus serotypes. The vaccine can encompass a single serotype or multiple serotypes and can be administered alone or with other vaccines.

Inventors: Baoming Jiang, Roger Glass, Jon Gentsch
CDC Reference Number: I-011-06

New Human Rotavirus Vaccine Strains - CDC-66 and CDC-81
The invention describes methods for adapting and producing human rotavirus vaccine strains to serve as an alternative to live oral rotavirus vaccinations and can prevent severe rotavirus diarrhea among children worldwide. The two new parenteral human rotavirus vaccine strains covered by this invention are representatives of common rotavirus serotypes. The vaccine can encompass a single serotype or multiple serotypes and can be administered alone or with other vaccines.

Inventors: Baoming Jiang, Roger Glass, Yuhuan Wang
CDC Reference Number: I-012-06

Licensing Opportunities

New biotechnology licensing opportunities are constantly being added to CDC's portfolio so be sure to visit our website often: www.cdc.gov/od/ads/techtran/index.htm

A blank Confidential Disclosure Agreement can be found on the last page of this brochure. Other forms are available upon request or can be obtained from the CDC website.

In addition, many other occupational safety licensing opportunities not included in this biotechnology brochure are available from CDC's Technology Transfer Office.

Questions about any of CDC's technologies may be directed to Suzanne Seavello Shope, J.D., Technology Licensing and Marketing Scientist, 770-488-8600 or SShope@cdc.gov.

TECHNOLOGY TRANSFER OFFICE

In 1986, Congress passed the Federal Technology Transfer Act (FTTA) to improve the link between the federal laboratories' technology base and U.S. businesses. This law and related legislation authorized federal laboratories to patent and license inventions to businesses, and to collaborate with commercial firms on research and development projects. These activities benefit the public by transferring scientific expertise and technology from government laboratories, thereby encouraging the development of improved health care products, processes, and services.

The Centers for Disease Control and Prevention (CDC) established a Technology Transfer Office (TTO) to implement the FTTA and related legislation, and to facilitate access to CDC's world renowned scientists, engineers and state of the art laboratories. The TTO manages CDC's and the Agency for Toxic Substances and Disease Registry's (ATSDR) intellectual property by administering technology transfer activities related to patents, trademarks, copyrights, trade secrets, licenses, biological materials licensing agreements (BMLAs) and cooperative research and development agreements (CRADAs) with the private sector and academia.

CDC's technology varies from discovery and early stage inventions, to commercially ready products. There are hundreds of partnering opportunities available to domestic and international corporations through the CRADA process. To learn more about CDC, please visit our web site at www.cdc.gov. You can also learn more about the technology transfer process at CDC by visiting the TTO web site: www.cdc.gov/tto.

The enclosed abstracts of CDC's patents and patent applications represent research and development activities from CDC's Centers, Institutes, and Offices:

Agency for Toxic Substances and Disease Registry (ATSDR)
Epidemiology Program Office (EPO)
National Center on Birth Defects and Developmental Disabilities (NCBDDD)
National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)
National Center for Environmental Health (NCEH)
National Center for Health Statistics (NCHS)
National Center for HIV, STD and TB Prevention (NCHSTP)
National Center for Infectious Diseases (NCID)
National Center for Injury Prevention and Control (NCIPC)
National Immunization Program (NIP)
National Institute for Occupational Safety & Health (NIOSH)
Public Health Practice Program Office (PHPPO)

Photo Credits
All photos used in this document were obtained from CDC's Public Health Image Library "PHIL™" (located inside CDC's website at http://phil.cdc.gov). We gratefully acknowledge the professionals who developed this library.

Technology Transfer Office Contacts
CDC - Mailstop K-79
4770 Buford Hwy
Atlanta, GA 30341
Main Phone (770) 488-8600
FAX (770) 488-8615
E-mail: tto@cdc.gov
www.cdc.gov/tto

Andrew Watkins, PhD, JD
Director
(770) 488-8610
E-mail: AWatkins@cdc.gov

Thomas E. O'Toole, MPH
Deputy Director
(770) 488-8611
E-mail: TOToole@cdc.gov

Suzanne Seavello Shope, J.D.
Technology Licensing and Marketing Scientist
(770) 488-8613
E-mail: SShope@cdc.gov

Russ P. Metler, RN, MSPH, JD
Patent Advisor
(770) 488-8604
E-mail: RMetler@cdc.gov

Sumita Chowdhury-Ghosh, J.D., Ph.D.
Patent Advisor
(770) 488-8612
E-mail: SChowdhuryGhosh@cdc.gov

Francisco (Paco) Candal M.S., MT(ASCP)
Patent Advisor
(770) 488-8608
E-mail: fjc1@cdc.gov

Catherine Lewis
Management and Program Analyst
(770) 488-8601
E-mail: CLewis@cdc.gov

Cynthia Robertson
Paralegal Specialist
(770) 488-8605
E-mail: CRobertson@cdc.gov

Veronica Brown
Technology Transfer Assistant
(770) 488-8600
E-mail: VBrown@cdc.gov

CONFIDENTIAL DISCLOSURE AGREEMENT

This Agreement is made by and between the Public Health Service ("PHS") and the company indicated below (hereinafter "Company").

In consideration of receiving for review from PHS a copy of the U.S. Patent Application(s) bearing the serial number(s) and title(s) indicated below (hereinafter "Application(s)"), Company agrees as follows:

1. Company agrees not to disclose any portion of the Application(s) to any third party without prior written permission from PHS, shall use reasonable care to maintain the confidentiality of the Application(s) with at least the same degree of care as is exercised in respect of Company's own proprietary information, and shall disclose the Application (s) only to those of Company's employees who have a need to review the Application(s) for the purposes specified in paragraph 4 below.

2. The following information categories are excluded from the confidentiality obligation of Paragraph 1:
   a. Information that was known to Company a bout the Application (s) prior to their disclosure under this Agreement;
   b. Information about the Application(s) that is or becomes generally available to the public through no fault of Company;
   c. Information about the Application(s) that is subsequently made available to Company from any third party that is not under a confidentiality obligation to PHS.

3. This Agreement does not grant an y license rights under the Application(s).

4. Company represents that the purpose of requesting the Application(s) is only to assess interest in obtaining a license under the Application(s). Company further represents that its request for the Application(s) is not to form the basis for filing a patent application or instituting any other proceeding in any patent office or court. Company agrees not to use the information contained in the Application(s) except for the p purposes stated in this Agreement.

5. Company's obligations under this Agreement shall remain in effect for seven (7) years from the date specified below.

6. Application(s) serial number(s) and title(s): U.S. Patent Application Serial No._____

   "_____," Our Ref.: I- -

UNDERSTOOD AND ACCEPTED BY COMPANY:

COMPANY: _____

BY: _____ Mailing Address: _____
Authorized Signature

_____ _____
Typed or Printed Name and Title

_____ _____
Date

This Page was Intentionally Left Blank

PUBLIC HEALTH SERVICE
BIOLOGICAL MATERIALS LICENSE AGREEMENT

This Agreement is entered into between the Public Health Service ("PHS"), through the Technology Transfer Office, the Centers for Disease Control and Prevention, Buford Hwy, Mailstop K-79 Atlanta, GA 30341, U.S.A. and

_____ ("LICENSEE"), a corporation of _____, having an office at_____.

1. DEFINITIONS

   a. **"Materials"** means the following biological materials including all progeny, subclones, and derivatives thereof: _____, as described in _____ and developed in the laboratory of _____.

   b. **"Licensed Products"** means _____.

   c. **"Net Sales"** means the total gross receipts by LICENSEE for sales of Licensed Products, or for income from leasing, renting or otherwise making Licensed Products available to others without sale or other disposition transferring title, whether invoiced or not, less returns and allowances actually granted, packing costs, insurance costs, freight out, taxes or excise duties imposed on the transaction (if separately invoiced), and wholesaler and cash discounts in amounts customary in the trade. No deductions shall be made for commissions paid to individuals, whether they be with independent sales agencies or regularly employed by LICENSEE, or for the cost of collections.

2. LICENSEE wishes to obtain a license from PHS to use the Materials provided under this Agreement in its commercial research or product development and marketing activities. LICENSEE represents that it has the facilities, personnel and expertise to use the Materials for commercial purposes and agrees to expend reasonable efforts and resources to develop the Materials for commercial use and/or commercial research.

3. PHS hereby grants to LICENSEE a worldwide , non-exclusive license to make , have made an d use the Materials and to make, have made, use and sell Licensed Products in the field of use of _____.

4. PHS agrees to provide LICENSEE with samples of the Materials, excluding progeny, subclones and derivatives thereof, ("Supplied Materials"), as available, and at reasonable cost to replace the Supplied Materials, as available, in the event of their unintentional destruction.

5. In consideration of the grant in Paragraph 3 above, LICENSEE hereby agrees to make the following payments to PHS:

   a. Within 30 days of its execution of this Agreement, a noncreditable, nonrefundable license issue royalty of _____Dollars ($_____).

   b. A nonrefundable minimum annual royalty of _____Dollars ($_____) which shall be due and payable on January 1 of each calendar and may be credited against earned royalties for due for sales made in that year. The minimum annual royalty for the first calendar year of this Agreement is due and pay able within thirty (30) days from the effective date of this Agreement and may be prorated according to the fraction of the calendar year remaining between the effective date of this Agreement and the next subsequent January 1.

   c. An earned royalty of _____ percent (___%) of Net Sales, which shall be due and payable within sixty days of the end of each calendar year.

All payments required under this Agreement shall be in U.S. Dollars, net of all non-U.S. taxes, and shall be made by check or bank draft drawn on a United States bank and made payable to "CDC/Technology Transfer" and shall reference the agreement number assigned by CDC. All payments required by this Agreement shall be mailed to the following address: CDC, Technology Transfer Office, 1600 Clifton Road, NE, Mailstop E-67, Atlanta, GA 30333. Late charges will be applied to any overdue payments as required by the U.S. Department of Treasury in the Treasury Fiscal Requirements Manual, Section 8025.40. The payment of such late charges shall not prevent PHS from exercising any other rights it may have as a consequence of the lateness of any payment.

6. LICENSEE agrees to make written reports to PHS within sixty (60) days after the end of each calendar year. This report shall state the number, description, and aggregate Net Sales of Licensed Products made, sold, or otherwise disposed of, and the total gross income received by LICENSEE from leasing, renting, or otherwise making Licensed Products available to others without sale or other disposition transferring title, during such completed calendar year, and resulting calculation pursuant to Paragraph 5 of payment due. LICENSEE shall submit each such report along with payment due PHS for the calendar year covered by the report to PHS at the address listed in Paragraph 5 above and shall also send a copy of the report to PHS at the Mailing Address for Notices indicated on the Signature Page of this Agreement. Late charges will be applied to any overdue payments as required by the U.S. Department of Treasury in the Treasury Fiscal Requirements Manual, Section 8025.40. The payment of such late charges shall not prevent PHS from exercising any other rights it may have as a consequence of the lateness of any payment.

7. LICENSEE agrees to supply the laboratory of Dr. _____ (PHS) at no charge reasonable quantities of Materials and Licensed Products that LICENSEE offers for sale or otherwise makes available for public use.

8. This Agreement shall become effective on the date when the last party to sign has executed this Agreement and shall terminate _____ ( ) years from this effective date, unless previously terminated under the terms of Paragraphs 16 or 17 below.

9. As part of LICENSEE's performance under this Agreement, LICENSEE agrees to _____

_____.

10. LICENSEE agrees to retain control over the Materials, and not to distribute them to third parties without the prior written consent of PHS except as provided in Paragraph 3.

11. LICENSEE agrees that this Agreement does not preclude PHS from distributing the Materials to third parties for research or commercial purposes.

12. By this Agreement, PHS grants no patent rights expressly or by implication to any anticipated or pending PHS patent applications or issued patents.

13. NO WARRANTIES, EXPRESS OR IMPLIED, ARE OFFERED AS TO THE MERCHANTABILITY OR FITNESS FOR ANY PURPOSE OF THE MATERIALS PROVIDED TO LICENSEE UNDER THIS AGREEMENT, OR THAT THE MATERIALS OR LICENSED PRODUCTS MAY BE EXPLOITED WITHOUT INFRINGING THE PATENT RIGHTS OF ANY THIRD PARTIES. LICENSEE accepts license rights to the Materials and Licensed Products "as is", and PHS does not offer any guarantee of any kind.

14. LICENSEE agrees to indemnify and hold harmless the United States government from any claims, costs, damages or losses that may arise from or through LICENSEE's use of the Materials or Licensed Products. LICENSEE further agrees that it will not by its action bring the United States government into any lawsuit involving the Materials or Licensed Products.

15. LICENSEE agrees in its use of any PHS-supplied materials to comply with all applicable statutes, regulations and guidelines, including Public Health Service and PHS regulations and guidelines. LICENSEE agrees not to use the Materials for research involving human subjects or clinical trials in the United States without complying with 21 CFR Part 50 and 45 CFR Part 46. LICENSEE agrees not to use the Materials for research involving human subjects or clinical trials outside of the United States without notifying PHS, in writing, of such research or trials and complying with the applicable regulations of the appropriate national control authorities. Written notification to PHS of research involving human subjects or clinical trials outside of the United States shall be given no later than sixty (60) days prior to commencement of such research or trials.

16. LICENSEE may terminate this Agreement upon sixty (60) days written notice to PHS.

17. PHS may terminate this Agreement if LICENSEE is in default in the performance of any material obligation under this Agreement, and if the default has not been remedied within ninety (90) days after the date of written notice by PHS of such default.

18. Upon termination of this Agreement, LICENSEE agrees to return all Materials and Licensed Products to PHS, or provide PHS with certification of their destruction.

19. Within ninety (90) days of termination of this Agreement, LICENSEE agrees to submit a final report to PHS, and to submit payment of any royalties due.

20. LICENSEE is encouraged to publish the results of its research projects using the Materials or Licensed Products. In all oral presentations or written publications concerning the Materials or Licensed Products, LICENSEE will acknowledge the contribution of Dr. _____ and the PHS agency supplying the Materials, unless requested otherwise by PHS or Dr. _____.

21. This Agreement shall be construed in accordance with the laws of the United States as interpreted and applied by the Federal courts in the District of Columbia.

22. This Agreement constitutes the entire understanding of PHS and LICENSEE and supersedes all prior agreements and understandings with respect to the Materials.

23. The provisions of this Agreement are severable, and in the event that any provision of this Agreement shall be determined to be invalid or unenforceable under any controlling body of law, such invalidity or unenforceability shall not in any way affect the validity or enforceability of the remaining provisions of this Agreement.

24. Paragraphs 9, 13, 14, and 20 of this Agreement shall survive termination of this Agreement.

SIGNATURES BEGIN ON NEXT PAGE

PHS BIOLOGICAL MATERIALS LICENSE AGREEMENT
SIGNATURE PAGE

In Witness Whereof, the parties have executed this agreement on the dates set forth below. Any communication or notice to be given shall be forwarded to the respective addresses listed below.

FOR **PHS**:

_____ _____
Date

Director
Centers for Disease Control and Prevention

Mailing Address for Notices: Technology Transfer Office
Centers for Disease Control and Prevention
4770 Buford Hwy
Mailstop K-79
Atlanta, GA 30341

FOR **LICENSEE** (Upon information and belief, the undersigned expressly certifies or affirms that the contents of any statements of LICENSEE made or referred to in this Agreement are truthful and accurate.):

_____ _____
Signature Date Date

_____
Printed Name

_____
Title

Mailing Address for Notices: _____

_____

_____

_____

APPLICATION FOR LICENSE TO PUBLIC HEALTH SERVICE INVENTIONS

Thank you for your interest in the technology transfer activities of the U.S. Public Health Service. Your answers to t he following questions will provide the foundation for licensing decisions. Please return this form and the required attachments to:

Technology Transfer Office
Centers for Disease Control and Prevention
4770 Buford Hwy
Mailstop K79
Atlanta, GA 30341

IDENTIFICATION OF INVENTIONS(S) FOR WHICH LICENSE IS SOUGHT (Complete all relevant sections)**:**

U.S. Patent Application(s) Serial Number(s), Filing Date(s), and Patent Number(s) (if issued):

Title of Patent Application(s):

Biological Material(s):

Inventor(s):

Source from which you learned of availability of a license to the present invention(s):

INFORMATION ABOUT APPLICANT:

Name & Address of Applicant:

Name, title, address, phone and FAX numbers of Applicant 's licensing representative:

Is Applicant a U.S. Corporation? _____ yes _____ no

If no, state country of origin: _____

State of incorporation or citizenship (if an individual): _____

Is Applicant a Small Business Firm? _____ yes _____ no

TYPE OF LICENSE SOUGHT:

_____ Exclusive Commercialization License

_____ Coexclusive Commercialization License

_____ Nonexclusive Commercialization License

_____ Nonexclusive Internal Commercial Use License (internal use only - no right to sell or otherwise distribute materials)

_____ Commercial Evaluation License

_____ Nonexclusive Biological Materials License (for a limited-term evaluation) (for materials not covered under a patent or patent application)

PROPOSED FIELD(S) OF USE:

ON *SEPARATE ATTACHMENTS* TO THIS APPLICATION, PLEASE PROVIDE THE FOLLOWING INFORMATION:

I. DESCRIPTION OF APPLICANT

Include nature and type of applicant's business; number of employees; corporate/divisional commitment to R&D, production, sales & marketing; financial resources; products or services successfully commercialized and any unique capabilities of your company relative to the licensed technology. (If a prior license application has been submitted to the Technology Transfer Office within the past year, you may reference that application for the company description.)

II. OTHER LICENSES AND USE OF THE INVENTION

Identify any licenses previously granted to the Applicant under federally owned invent ion s. Also, identify, to the best of Applicant's know ledge, the extent to which the invention for which a license is sought is being practiced by private industry or Government, or is otherwise available commercially.

III. PROPOSED LICENSE TERMS

Include definitions of licensed products, processes or methods; geographic territories; duration of license; claims (if known) of patent /patent application under which the proposed licensed technology would fall; and other terms for which you wish to make a proposal at this time.

IV. RESEARCH, DEVELOPMENT AND MARKETING PLAN

Include description of product(s) or method(s) to be developed with the licensed technology and, for each product or method to be developed, a description of expected product research and development programs, including (where relevant) major preclinical, clinical, regulatory, manufacturing and marketing stages; monetary and personnel commitments for each development stage; and the projected time to accomplish each stage of commercial development. *If you will be using the licensed technology in house but will not be directly commercializing the licensed technology or providing a service based on the technology, you need only describe the research program in which the licensed technology will be utilized.*

V. MARKET ANALYSIS

Include relevant market segment (s) the licensed technology will serve when commercialized; market size and projected growth of relevant markets during the duration of the license; estimated market share once product is introduced; and sales projections based on market share analysis. *(THIS INFORMATION NEED NOT BE PROVIDED IN APPLICATIONS FOR COMMERCIAL EVALUATION LICENSES OR NONEXCLUSIVE COMMERCIAL RESEARCH LICENSES.)*

VI. OTHER INFORMATION WHICH YOU BELIEVE WILL SUPPORT A DETERMINATION TO GRANT THE REQUESTED LICENSE

VII. FOR APPLICANTS FOR EXCLUSIVE OR PARTIALLY EXCLUSIVE LICENSES ONLY

A detailed statement as to *1)* why Federal and public interests will be best served b y exclusive licensing of this invention; *2)* why expeditious practical application of the invention is unlikely to occur under a nonexclusive license; *3)* why the exclusive licensing of this invention is a reasonable and necessary incentive to attract investments of risk capital; *4)* why the exclusive licensing of this invention will not tend substantially to lessen competition or result in undue market concentration; and *5)* why the proposed license terms and scope of exclusivity are not greater than reasonably necessary.

I certify, to the best of my knowledge, that all of the information provided on this application and on attachments to this application is true and accurate.

_____ _____

Signature of Applicant or Authorized Representative Date

_____

Print Name and Title

The commercial and financial responses in this application will be treated as privileged and confidential information as provided in 15 U.S.C. 209(a); and, to the extent permitted by law, will not be accessible under the Freedom of Information Act.